CLINICAL MODEL OF IMMUNOLOGICAL TRANSFER FROM THE MOTHER TO THE NEWBORN AFTER VACCINATION AGAINST SARS-COV-2 DURING PREGNANCY

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Abstract

Coronavirus disease represents a new and extremely contagious infectious entity, declared a pandemic in March 2020. Pregnant women confirmed with COVID-19 can develop severe forms of disease, being at greater risk of ICU admission, preterm birth occurring 3 times more frequently for this category. Initially, pregnant women were excluded from phase 3 vaccine clinical trials, thereby not enough data about the safety and efficiency of vaccination against COVID-19 is available. Currently, the producing companies have several ongoing studies. Under these circumstances, we present the case of a newborn from a young mother with no known pathologies, with no reported infection throughout the pregnancy and vaccinated with Pfizer-BioNTech vaccine at 31 and 34 weeks of pregnancy, respectively. Anti-spike antibody serum and breast milk concentrations were determined. This case indisputably demonstrates the existence of an important specific antibody transfer from the mother to her offspring, both by transplacental and human milk passage.

Keywords: SARS-CoV-2, pregnancy, vertical transmission, newborn, vaccine, spike protein

Introduction

Coronavirus disease appeared in China by the end of 2019 and rapidly spread throughout the world, being declared a pandemic in March 2020.

Many scientists joined forces to discover a vaccine that could put an end to pandemic evolution as quickly as possible and save the population. Generally, the main purpose of vaccines is to create a host immune response (defense), so that it can develop B and T cell immunological memory against an infectious agent (in the case being, SARS-CoV-2 virus). The development of immunological memory after vaccination is the one that will protect from further infections [1]. All scientist efforts led to the production of 6 vaccines, using different technologies (classical and modern methods). The COVID-19 pandemic set out the development of new vaccine production technologies, some of which had never been human tested before, such as DNA and mRNA based. Until recently, most vaccines were working by infectious agent inoculation into the human body, in order to induce immune response. The antigen was represented either by the inactivated (prior to inoculation) infectious agent, or by a purified protein belonging to the pathogen. Using the modern biotechnology and genetic engineering, large quantities of viral DNA and RNA can be obtained, requiring only the sequence of genetic material of the SARS-CoV-2 virus, this being made public by the Chinese researchers on 11th of January 2020 [1,2]. Unlike classic vaccines, the ones produced by Pfizer-BioNTech and Moderna work by transporting the genetic information required for the synthesis of SARS-CoV-2 spike protein, which can be naturally found on the viral surface. After vaccine inoculation, the muscle cells produce the spike protein, which is then recognized by the immune system. After a couple of days, the mRNA is degraded into the cytoplasm and does not enter the nucleus, which means it is not integrated in the cellular DNA [3,4]. The Astra-Zeneca Oxford and Janssen-Johnson and Johnson vaccines use a modified viral vector that can deliver the spike protein into the cell, triggering the immunologic response. These 4 vaccines are largely used across the USA and Europe and so, with the help of vaccination, millions of people have been able to protect themselves against this disease [1].

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Pregnant women that develop COVID-19 can present with severe forms of disease, especially if comorbidities are present, or associated to pregnancy (high blood pressure, diabetes, obesity, asthma etc.). These cases have higher risks of ICU admission and preterm delivery risk is 3 times higher compared to pregnant women who did not contract or develop the infection [5]. Initially, pregnant women were excluded from the vaccines clinical trials, this being the main reason why there is still insufficient data reported about the efficacy and safety of vaccinating against COVID-19 during pregnancy [6]. At this time, there are several ongoing studies, done by the producing companies. During pregnancy, most vaccines can be administered if the benefits overcome the risks [7]. Vaccines against flu, tetanus, diphtheria and pertussis are frequently used during pregnancy, due to the protection they, by transplacental antibody transfer from the mother to the fetus/newborn [5]. Starting from these unanimously approved results, we expect the vaccine against COVID-19 to offer the same anti-infectious protection to both the mother and the fetus/newborn [5,6,7].

Material and method

After maternal vaccination during pregnancy, anti-Spike (S) protein antibody titer was determined, from the maternal and neonatal blood, as well as from breast milk. For anti-S protein antibody determination, the ECLIA (electrochemiluminescence) method was used, an immunologic test that allows the quantitative analysis of IgG antibodies against SARS-CoV-2 S protein receptor binding domain (RBD) in both human serum and plasma, as well as human milk. The test is suggested as an adjuvant for the evaluation of humoral immune reaction to SARS-CoV-2 S protein.

Case report

We present the case of a 24 years old pregnant woman from Timișoara, Romania, Gravida 1, Para 1, with no history of SARS-CoV-2 infection and who decided, together with the family and obstetrician, to vaccinate against COVID-19.

The pregnancy developed as a physiological process, within normal parameters, with no preexistent pathologies or complications. The fetal evolution and development were normal, both before, as well as after vaccination. The main reason for vaccine uptake was due to the fearful complications the disease can cause, having a husband who was working in an environment with high infection risk and also for being a General Medicine student.

By 31-weeks gestational age, the first dose of Pfizer-BioNTech vaccine was administered, and by 34-weeks the second dose, as well. No adverse effects were reported other than local pain surrounding the inoculation area. No analgesics or antipyretic medication was administered neither before nor after vaccination. Following vaccination, the evolution of pregnancy developed within normal ranges, with on-time check-ups and prenatal care, which showed normal fetal growth and development.

By 39-weeks gestational age, spontaneous labor occurred, followed by normal vaginal delivery, in cephalic presentation, from which resulted a newborn with appropriate gestational weight (3500g), length (51cm), head circumference (35cm) and an APGAR score of 10. The neonatal adaptation to the extrauterine life was normal. According to the hospital's protocol, the pregnant woman was tested against COVID-19 on admission, by polymerase chain reaction (PCR), with a negative result.

After delivery, the usual laboratory tests of the mother and neonate were normal, with no pathologic findings. In the 5th day after delivery, both the mother and her newborn came into our clinic for a usual check-up, which showed a normal newborn evolution and for several tests, which included specific anti-SARS-CoV-2 antibodies (IgG and IgM) testing from the venous blood, that were negative, meaning the infection never occurred. At the same time, the anti-Spike (S) protein antibody titer was determined, from the maternal and neonatal blood, as well as from breast milk. For anti-S protein antibody determination, the ECLIA (electrochemiluminescence) method was used, an immunologic test that allows the quantitative analysis of IgG antibodies against SARS-CoV-2 S protein receptor binding domain (RBD) in both human serum and plasma, as well as human milk. The test is suggested as an adjuvant for the evaluation of humoral immune reaction to SARS-CoV-2 S protein. The minimum detection limit, under which the result is negative for the presence of antibodies against the S protein represents 0,80U/ml, above this value the result being positive.

Results

The antibodies against Spike protein of SARS-CoV-2 evaluated 5 days after delivery from the maternal and neonatal serum were increased, the maternal titers were of 624U/ml and the neonatal ones of 470U/ml. The titers from human milk were lower, of only 1.34U/ml, but above the minimum detection limit. A follow-up of anti-spike antibody titer dynamics, 6 weeks after delivery (and 5 weeks after the first determination) was done. The antibody titers from the maternal and infant blood and from human milk were once again determined. The results were increasingly higher for the mother, with values of 737.2U/ml (serum value) and 1.61U/ml (breast milk value), which translates to a more important antibody transfer via human milk. Although the infant's antibody titer was lower (164.9U/ml), its value is still appropriately increased for offering a sufficient anti-infectious protection by 4 months of age, when the infant's immune system starts to produce its own antibodies. The finding of this type of antibodies in human milk is both important and benefic due to the fact that this transfer can never be a passive one, but one that contributes to the anti-infectious mucosal defense, taking into account that an exclusively breastfed newborn can ingest up to 800-1000 ml of human milk in 24 hours.

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Antibody titer (U/ml)		
	5 days	**6 weeks**
Mother serum	624	737.2
Breast milk	1.34	1.61
Newborn/Infant serum	470	164.9

Table 1. Table demonstrating antibody titers from the maternal, neonatal/infant serum and breast milk

Discussion

The development and apparition of mRNA based vaccines stands upon research initiated since 2006 and finished after 15 years, with the launch of 2 vaccines, Pfizer-BioNTech and Moderna, respectively. These vaccines represent a premiere in vaccinology and the pressure exerted by the SARS-CoV-2 pandemic represented a good opportunity for this type of vaccines, so they could contribute significantly and put an end to this pandemic [3,4].

The vaccination of pregnant women leads to cellular and humoral mediated immunity, which increases the resistance against infection and reduces the vertical transmission rate [3,7,8]. Furthermore, vaccination produces IgG antibodies, which can cross the placental barrier and IgG, IgA and IgM antibodies which have a role in mucosal immunity and are secreted in colostrum/mature breast milk, and then ingested by the newborn during breastfeeds [9,10,11].

Anti-Spike antibodies acquired after vaccination and found in human milk, even if they appear in reduced quantity, are accumulated by administration repetitivity, when the newborn and infant is exclusively breastfed. As mentioned above, the breastfed newborn can ingest around 800-1000ml of milk per day, which ensures an immunologic overprotection if we add the antibodies transferred through the placenta during pregnancy [11]. The anti-Spike antibody transfer via breastmilk is followed by a subtler cell transfer, with cells both involved in anti-infectious defense as well as memory cells, which will contribute to the infant's future immune mechanisms. Lately, affirmations regarding the colostrum and mature milk cellularity, based on scientific arguments, strongly suggest that no milk contamination takes place, but a highly-selective immunological transfer with an essential role in the mucosal anti-infectious defense, including respiratory mucosa, which is greatly affected by the coronavirus infection [12,13].

In the above presented case we indubitably demonstrated that the anti-Spike antibodies acquired after vaccination against SARS-CoV-2 virus can cross the placental barrier from the maternal blood to the fetus. The pregnant woman was vaccinated with 8 and 5 weeks prior to delivery, which allowed enough time for the production, development and transfer of protective antibodies. During the first determination (5 days after birth) the plasmatic antibody quantity present in newborn represented 75% of the maternal plasmatic antibody titer, which leads to the conclusion that there exists a significant and sufficient placental and breastmilk antibody transfer for the protection of both the newborn and infant, at least until 1 year of age, which determines ab initio the exclusion of vaccination during the first year of life. The maternal plasma antibody titer had an increase of 18,1% from the first determination, fact that directly correlates to an equal increase in maternal breastmilk antibody titer, which was 20% since the first determination.

Conclusions

The most authorized recommendations for vaccination against COVID-19 during pregnancy come from the American College of Obstetrics and Gynecology (ACOG), which recommends that the vaccine should not be contraindicated during pregnancy and the decision must be taken together with the obstetrician.

World Health Organization considers there are no specific risks that outweigh the benefits of vaccination for pregnant women. The pregnant women at high risk of SARS-CoV-2 exposure (health care workers), or the ones with associated comorbidities (conditions that can lead to death) can be vaccinated after an accurate assessment done by the obstetrician, with interdisciplinary collaboration, if the case presents, with other specialties.

This paper illustrates that vaccination during pregnancy and breastfeeding provides the infant immunity during the first 4-6 months of life.

There is a significant and urgent need of research regarding the effectiveness and safety of vaccination against SARS-CoV-2 during pregnancy and establishing the optimal period of time for the vaccine administration, both for the mother as well as her fetus/newborn.

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