Journal of Clinical Immunology Research

Extended Abstract
Vol. 3, Iss. 1
2020

World Vaccine Meet 2019: BCG vaccine and Immunodeficiency -Daifulah ALZAHRANI-National Guard hospitals, Jeddah, Saudi Arabia

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Tuberculosis (TB) is considered by WHO as global health emergency in 1993. In 2011 one third of the world's population was thought to be infected with TB and 8.7 million cases of active TB annually.BCG vaccine is one of the effective control measures to prevent TB. It is in practice since 1960s where TB is highly prevalent and 120 million BCG vaccines are given annually, that is effective in preventingsevere disease of extrapulmonaryTB.However, BCG vaccine is live attenuated vaccine that potentially could cause infection, with an incidence between 1:10,000 to 1:1,000,000 and significantly higher when given to immunodeficientinfants. Immunodeficient infants who take BCG vaccine at birth could develop circulated BCGitis, which is corelated with high morbidity and mortality. However, those who develop disseminated BCGitis usually require hospital admissions and multiple medications with high cost and low survival rate ranging between 0% to 65% worldwide.Our center; KAMC-WR, Jeddah Saudi Arabia, has 83% survival rate of treating patients with disseminated BCGitis, but with using cytokine therapy and aminoglycoside drug in addition to common anti-TB drugs. Vaccination policies vary around the world, linked mostly to tuberculosis disease prevalence. While tuberculosis native areas (mainly in developing countries) approve universal vaccination, tuberculosis low-prevalence countries either restrict BCG vaccine to high-risk groups or choose not to administer it at all . Controversies surrounding the vaccine's efficacy account for variations in vaccination policies. While BCG vaccine is trusted to provide a consistent protection against severe forms of tuberculosis (i.e., miliary, meningeal) in childhood, most adult individuals remain susceptible to pulmonary tuberculosis in spite of vaccination. As previous exposure to non tuberculous mycobacteria (NTM) seems to influence vaccine efficacy, and to assure full coverage, BCG is usually given right after birth in the first months of life. Even in the context of its questionable efficacy, BCG vaccine is considered safe in immunocompetent subjects. However, being a live vaccine, it can result in serious illness or even fatal disease in immunocompromisedhosts . For instance, WHO directions recommend holding BCG vaccination in high-danger infants until assessment of HIV status. Patients with dominant immunodeficiency diseases (PIDD) are at balance or even greater hazard of complications and represent a challenging group regarding live vaccines in general and BCG vaccination in particular.

There is high rate of constitutional immunodeficiency diseases (PID) in the Middle East and ministry of health in Saudi Arabia recently succeeded in moving the BGC vaccine to 6-month of age, instead of giving it at birth, in order to have time for diagnosing PID.WHO considers the development of new TB vaccines a major public health priority. An extensive regulated questionnaire evaluating complications, outcomes.and therapeutics regarding BCG vaccination in patients given a diagnosis of SCID was extensively distributed. Summary data and association analysis was performed. Tuberculosis is a most global health problem. In 1993 the WHO declared the disease a global public health emergency and in 2011 one third of the world's population was thought to be infected with Mycobacterium tuberculosis with almost 9 million new cases diagnosed and 1.4 million deaths attributed to this organism. In recent years, most technologically advanced countries have managed to control— although not eradicate—tuberculosis. With over 4 billion doses applied, the live-attenuated M. BovisbacilleCalmette – Guérin (BCG) vaccine has been a part of efforts to control tuberculosis and worldwide remains one of the most widely used of all current vaccines. Since the 1960s it has been given routinely in the majority of countries and currently approximately 120 million people -mostly newborns- are vaccinated every year through national childhood immunization programs. The BCG vaccine has a

The work is partly presented at World Vaccine and Immunology Conference on November 21-22, 2019 held at Dubai, UAE

chronical protective effect against meningitis and ciruculated TB in children, however it does not limit primary infection and, more importantly, does not prevent reactivation of latent pulmonary infection, the principal source of spread in the community. The impact of BCG vaccination on transmission of M. Patients who were immunized at birth with BCG and who developed a propagated infection are reported to emphasize the importance of taking an extensive medical history before giving the BCG vaccine. Patient 1 has a relative who had familial hemophagocyticlymphohistiocytosis. Patient 2 has a harsh immunodeficiency with deep lymphopenia. Patient 3 has a sibling who had a scatter BCG infection. Patient 4 has two relatives with an immunodeficiency clutter; one sibling passed away in infancy and one is receiving daily immunoglobulin infusions. Patient 5 has deep lymphopenia and his brother had cytomegalovirus (CMV) pneumonitis and passed away in inception. Severe combined immunodeficiency disease (SCID) includes a heterogeneous group of genetic conditions characterized by profound deficiencies of T (and in some types, B and/or NK cell) numbers and function. If unprocessed, infants with typical SCID surrender early in life from severe and repeating infections. Mutations in different genes affecting cytokine signaling (e.g., IL2RG, and IL7RA), antigen receptor processing (e.g., RAG1, RAG2, and CD3δ) or nucleotide processing (e.g., adenosine deaminase – ADA-) cause this fatal childhood condition, unless immune reconstitution can be accomplished4. However, it should be noted that individuals with severe manifestations of other syndromic conditions may have clinical signs and symptoms consistent with SCID5. BCG, as other live-attenuated vaccines, is absolutely contraindicated in SCID patients (reviewed in1,6, and Global Tuberculosis Report, 2012, World Health Organization. However, because it is usually administered at birth, SCID patients in most countries using BCG are vaccinated before their immune deficiency is diagnosed.

Conclusion:BCG vaccine is one of the effective preventive measures of TB, however, it could cause serious complications with low revival rate. Moving the BGC vaccine to 6-month of age will give time for diagnosing PID.Using cytokine therapy and aminoglycoside drug in addition to common anti-TB drugs will significantly reduce mortality and morbidity. These adverse events could have been avoided by accumulate the relevant clinical and laboratory information. These cases also underscore the importance of a strict adherence to the BCG vaccine policies. Local and international archives that measure the birth prevalence of primary immune deficiencies are needed earlier to implementing universal BCG vaccination organization. BCG vaccine has a very high rate of obstacles in patients with SCID, which rise morbidity and mortality rates. Until safer and more adequate anti tuberculosis vaccines become available, lag in BCG vaccination should be considered to protect highly accessible populations from preventable complications. There are potentials for development of new BCG vaccine.

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