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COMMENTARY

Vaccine repurposing approach for preventing COVID 19: can MMR vaccines reduce morbidity and mortality?

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ABSTRACT

The coronavirus disease (COVID-19) is resulting in millions of infected individuals with several hundred thousands dead throughout the world. Amidst all the havoc, one interesting observation in the present COVID-19 pandemic is the negligible symptoms in the young; particularly children below 10 years of age. We assume the extensive pediatric vaccination with MMR vaccines followed globally could have resulted in innate immune responses, e.g., induction of interferons (IFNs) and activated natural killer (NK) cells, thereby offering natural immunity against SARS-CoV-2 in the young population. Possible cross-protective innate immunity offered by MMR vaccination prompted us to suggest repurposing MMR vaccination for immuno-prophylaxis against COVID-19.

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COVID-19 pandemic and therapeutic crisis

The present pandemic of coronavirus disease (COVID-19) has been creating havoc worldwide, causing an unprecedented crisis in every sector. Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is highly infectious as indicated by the millions of infected individuals in almost all countries with 100,000 s dead, mostly from developed nations.[1]

No standard treatments are available against SARS-CoV-2; several clinical trials are investigating repurposed drugs. Besides, the uncertainty of these drugs in terms of their anti-viral properties, adverse effects associated with drugs such as hydroxychloroquine have been documented.

Key features of COVID 19

One of the intriguing features of this viral disease is its preferential targeting of elderly and adult population with underlying morbidities compared to healthy young individuals who usually have very mild or no symptoms. This observation has prompted probing pathogenesis. Although immuno-pathogenesis is a plausible theory with this clinical scenario, there are several unanswered questions in that the clinical features associated with morbidities and mortalities do not follow a pattern and thus therapeutic options are followed by a case-by-case approach. This is also reflected with an increased morbidity and mortality in immunosuppressed conditions such as cancer patients and individuals with life-style disorders.

Does the low prevalence in children suggest possible solutions?

Even though COVID 19 is impacting all aspects of life, the interesting scenario is the negligible symptoms in the young; particularly children below 10 years of age, even though this age group is the most susceptible to most infectious diseases.[2] Our assumption is that the extensive pediatric vaccination schedule followed globally could have resulted in innate immune responses, e.g., induction of interferons (IFNs) and activated natural killer (NK) cells, thereby offering natural immunity against SARS-CoV-2. Most vaccination schedules have Mumps, Measles, and Rubella (MMR) vaccination for children. MMR vaccine consists of attenuated enveloped RNA viruses that have glycoprotein spikes, similar to SARS-CoV-2. Consequently, there might also be some antibody-mediated cross protection, given with 32%, 31%, and 33% similarity between the spike glycoprotein sequences of measles, mumps, and rubella, respectively, with SARS-CoV-2 glycoprotein. Hence, the chances of cross-protection provided by MMR vaccination may be higher as a combined effect of IFNs and NK cells with strong anti-viral activities and the cross-reactive antibodies.

Interferons and natural killer cells

IFNs are a heterogeneous class of soluble glycoproteins with strong antiviral activities. IFN production within immune-competent cells is triggered in response to viral and intracellular bacterial infections. Leukocytes, fibroblasts and NK cells synthesize IFN-α, IFN-β, and IFN-γ, respectively. There are 13 IFN-α genes and 1IFN-β gene, both lacking introns and encoded in the short arm of human chromosome 9, while the IFN-γ gene has three introns and is present in the long arm of chromosome 12.[3]

NK cells have the ability to recognize and lyse a wide array of target cells that include tumor cells and virus-infected cells. Studies on NK cells suggest that there is an increased activity of

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these cells in viral infections which provides a first line of defense. Experimental animal models with a wide range of viral infections show activation of NK cells with an important role in recovery from these infections. Furthermore, NK cells also have major roles in limiting the severity and duration of viral infections. It is noteworthy that viral vaccines induce NK cell proliferation in humans in the absence of clinical infection and such NK cell responses are more robust and long-lasting. Thus, enhancing NK cell activity by administering viral vaccines is suggested as a potential therapeutic option to prevent serious viral infections.[4]

Benefits of vaccination in arresting the cytokine storm

Pathogenesis involved in severity and mortality associated with COVID-19 cases is thought to be tied to the cytokine storm which includes the production of pro-inflammatory cytokines (IL-1β, IL-6, IL-12, IL-18, IL-33, TNF-α, TGFβ-) and that includes IFN and NK cell production, thereby raising the question of their protective role. However, experimental studies have shown that vaccination followed by reinfection stimulates only very low levels of cytokine production, which may result in mild or asymptomatic infections.[5] This might explain the mild or asymptomatic SARS-CoV-2 infections in children worldwide who had recent vaccinations particularly viral.

Limitations of therapeutic IFNs and NK Cells

Several studies indicate the usefulness of IFNs in the treatment and control of viral infections. However, the treatment of virally infected individuals with therapeutic IFNs has often resulted in undesirable side effects; harmful reactions have been reported in almost all organ systems.[6] Moreover, cost constraints prevent the use of expensive therapeutic IFNs in developing countries. Similarly, therapeutic application of NK cells for the management of cancer patients is hampered due to complexities in donor immunogenetics and availability.

MMR vaccines might offer hope

The preponderance of measles deaths (>140,000 in 2018) globally in children under the age of five triggered increased uptake of MMR vaccine, which has reduced cases in the recent past. Interestingly, IFNs elicited by vaccine strains are reported to be more efficient in offering protection than wild-type disease strains. Similarly, vaccine-induced NK cells are more potent and robust in their antiviral activities.[7] Thus, coupled with the advantage of vaccine-induced IFNs, NK cells, and the cross-protective antibodies, successfully exploiting this mechanism could prevent or ameliorate SARS-CoV-2 infection.

SARS-COV-2 vaccine development has been underway in earnest, with groups using various platforms such as mRNA, DNA, subunit, protein-based, viral vectors, live-attenuated, and inactivated vaccines. Nevertheless, we cannot predict how long it will take for these vaccines to be shown to be safe and effective and to become licensed for the general population.

Commonalities between the MMR viruses and SARS-COV -2 in terms of transmission and their primary replication in the upper respiratory tract, and possible cross-protective innate immunity offered by vaccination prompt us to suggest repurposing MMR vaccination for both prophylaxis and preventing the transition of less severe to life-threatening complications of COVID-19. Prevalence of COVID-19 disease and their complications in adults sparing the children, clearly gives us a lead to consider clinical trials vaccinating adults including healthy and vulnerable population with underlying co-morbidities irrespective of their prior vaccination status as a simple prophylactic strategy. This will save time and resources in that MMR vaccine is readily available, inexpensive, very safe FDA-approved and easy to administer, which could result in sparing some of the morbidity and mortality associated with SARS-CoV-2 infection.

Disclosure of potential conflicts of interest

We declare that there is no conflict of interest

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