ACHSM Asia-Pacific Journal of Health Management

COMMENTARY

REPURPOSING OF POLIO VACCINE IN PREVENTION OF COVID-19: THINKING TOWARDS MORE OPTIONS

Sunil Kumar[1], Dharmendra Pandey[1], Awanish Kumar[2]*

1. Faculty of Biosciences, Institute of Biosciences and Technology, Shri Ramswaroop Memorial University, Barabanki, Uttar Pradesh, India
2. Department of Biotechnology, National Institute of Technology, Raipur, Chhattisgarh, India

Correspondence: drawanishkr@gmail.com

ABSTRACT

COVID-19 has created an unprecedented crisis worldwide in every sector. There currently is no approved drug available against this disease. The development of a vaccine is also a complex and long process that is often completed in 10-15 years. Recently, several vaccines for COVID-19 have received emergency approval for use but few experts deem that currently approved COVID-19 vaccines might provide a temporary boost to the immune system, but they are dubious for their long-term effect and safety. This article sheds light on polio vaccine as a possibility on COVID-19 prophylaxis because this vaccine was developed through a rigorous process of the various phases of development. The polio vaccine could provide another option to combat COVID-19 and if we have more options, we can fight more effectively against the pandemic. The polio vaccine is utilized globally with a highly satisfactory retort and very good immune responses. By seeing a satisfactory cross-protective immune response, the polio vaccination could be repurposed and offered against COVID-19 for an effective immuno-prophylaxis and protection. This article focusses on the repurposing of vaccines/drugs for COVID-19 and discusses the scientific rationale behind the suggestive use of the polio vaccine against COVID-19 because the polio vaccine is FDA-approved less expensive, readily available, easy to administer, and highly safe.

KEYWORDS

COVID-19; Vaccine repurposing; Polio vaccine; Immuno-prophylaxis against SARS-CoV-2; More prophylactic option

INTRODUCTION

The COVID-19 (coronavirus disease-2019) pandemic has impacted all aspects of our life for the past two years. The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is an etiologic agent of COVID-19 that has infected millions of people globally and put unprecedented strain on healthcare systems [1–4]. Co-infections are a common consequence [3, 5], especially with longer hospital stays [6]. This coronavirus illness is worldwide disseminated and has predisposed a relatively high proportion of individuals to acute respiratory distress syndrome. While the world waits for a fully verified vaccine of COVID-19, some experts believe that current vaccinations might provide a much-needed temporary boost to the immune system in order to prevent infection. It is still unclear if such an approach would work, and some authorities are skeptical. Others, including Israeli, Dutch, and Australian researchers, are

investigating that a TB vaccine may help jump-start the immune system and make COVID-19 less dangerous, however, the WHO strongly recommends against using it until it has been shown effective against the COVID-19 disease.

COVID-19 has created a global healthcare emergency, particularly for poor countries like India, which have inadequate healthcare resources and a patchwork healthcare infrastructure. Given that we are in a pandemic, it is critical to investigate the potential of repurposing existing vaccinations. A recent epidemiological study reported that live-attenuated vaccinations (LAV) such as the Bacillus Calmette-Guérin (BCG) measles vaccine and oral polio vaccine (OPV) may induce non-specific immune responses after single or double doses and may protect against different viruses [7-13]. Furthermore, Mayo Clinic retrospective research found that those who have had previous OPV immunizations over a 1-, 2-, or 5-year period have a reduced incidence of SARS-CoV-2 infection than for people who have not been vaccinated yet [14].

The return of COVID-19 in India and in some other countries has resulted in an upsurge in the number of pediatric COVID-19 patient hospitalizations [15]. It may be claimed that because the majority of these individuals were vaccinated with OPV and BCG as part of the National Immunization Schedule, the predicted cross-protection from OPV against SARS-CoV-2 may not occur. However, anecdotal data suggests that the relative COVID-19 severity in pediatric instances is lower than in adult cases, even in the second wave, and it's possible that innate immune system activation plays a role in partial immunity to severe COVID-19 in pediatric cases. The possible reason behind this is there was extensive Polio vaccination done in children globally that could have resulted in innate immune responses [activated natural killer (NK) cells and induction of interferons (IFNs)] which offer a natural immunity against SARS-CoV-2 in children. So if the Polio vaccine is offered to the adult population, it will surely confer cross-protection in adults against SARS-CoV-2.

After entering its third phase, which includes all people over the age of 18, the world is presently experiencing severe shortages in order to carry out an ambitious universal COVID-19 immunization push. In such cases, innate immune system reactivation with a LAV like OPV could hypothetically act as partial immunity against COVID-19 until available vaccines become widely available and can boost the immune response subsequently with a combination of OPV, or inactivated vaccine category of the three COVID-19 vaccine candidates that OPV, LAV, and an adenovirus vector-based. We attempt to spotlight discussion on some available data and scientific reasons for the potential use of Polio vaccination against COVID-19 in this paper.

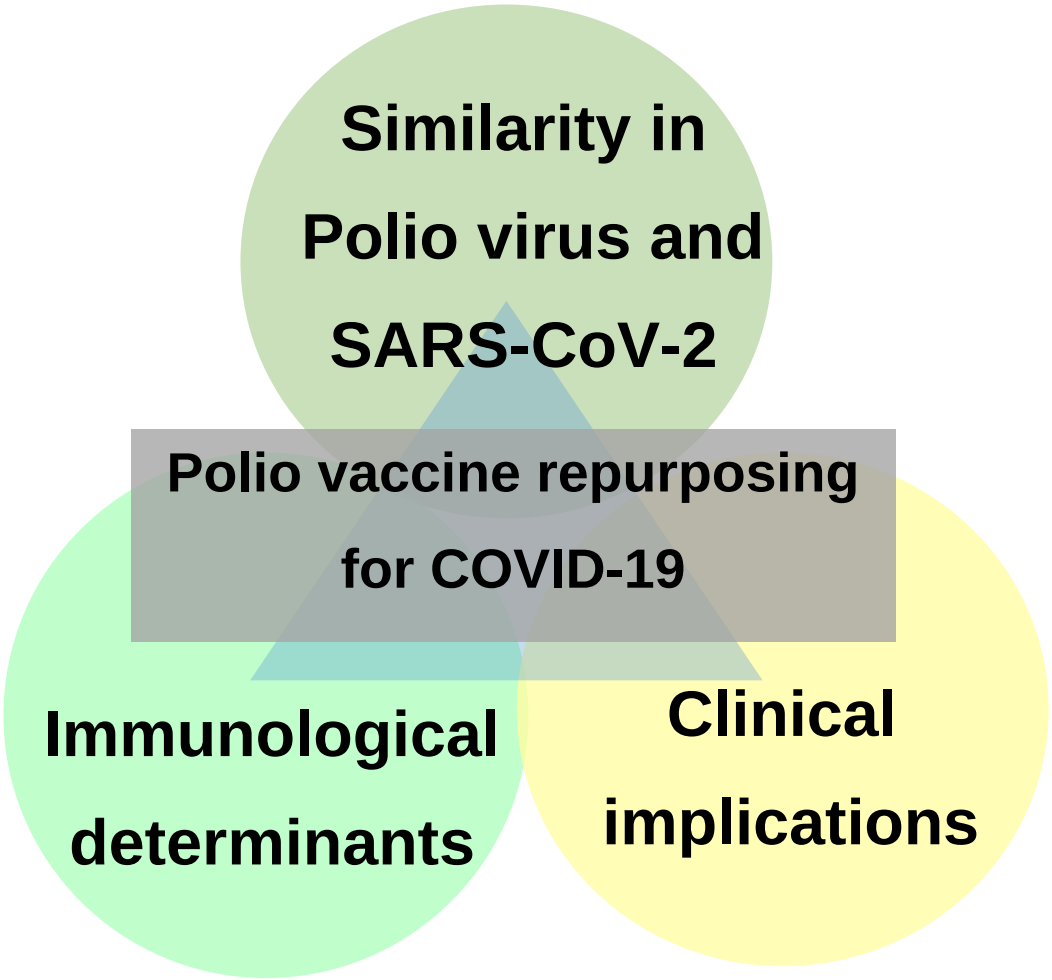
CURRENT THERAPEUTIC STATUS AND REPURPOSING OF VACCINE/DRUG FOR COVID-19: IN BRIEF

Currently, there is no dedicated drug available for COVID-19 treatment. The current research and development (R&D) of drugs and their production timelines are not conducive to give any quick responses to COVID-19 pandemic threats. Anti-COVID-19 drugs are in the development phase and may take a few years to come into the global market [16]. Since the process of research and working on new content is time-consuming, expensive, and needs regulatory approvals, therefore repurposing could shorten the time and reduce the cost of the vaccine and drug discovery [17]. Repurposing of vaccines and drugs may give relief for the current pandemic because repurposing of vaccines/drugs, represents an effective strategy to use existing vaccines/drugs to combat the unknown threat. Opinions of researchers have demonstrated that some existing vaccines (like Polio and BCG) may protect against other viral infections of the respiratory tract. A Phase 3 randomized double-blind trial of oral polio vaccine was completed, and its efficacy and safety studies were also performed for COVID-19 [18]. The trial of the BCG vaccine to check its efficacy against COVID-19 has begun with the collaboration of four countries Australia, Germany Netherlands, and United Kingdom [19]. These steps could be useful because in the present situation active research seeks to hasten and strengthen vaccine development for COVID-19. After all, significant vaccination is needed in society to achieve herd immunity against COVID-19. Some vaccines for COVID-19 received emergency approval and some are under a development phase. Polio and BCG vaccines may offer a new potential tool in dealinf with COVID-19 because they are safe and approved already.

Repurposing drugs would be another potent strategy to treat common and rare diseases like COVID-19. Repurposing of drugs is strongly advocated because it offers the use of risk-addressed compounds that can be developed in shorter timelines with lower costs.

Hydroxychloroquine (an analog of chloroquine) is a popular and approved antimalarial drug which was found to be efficient on nCOV and reported to be effective on COVID-19 patients in China, USA, and other countries [20]. In the direction of repurposing, a recent powerful network-based study was performed with some repurposed drugs (e.g., sirolimus, mercaptopurine, and melatonin) for rapid identification of a potential drug against COVID-19 [21]. A trial of the antiviral drug Lopinavir–Ritonavir was undertaken in adult hospitalized patients in China, but no significant result was observed in severe COVID-19 patients [22]. However, repurposing/testing of some other antiviral agents like Favipiravir, Remdesivir, and other classes of drugs is warranted in the future to anticipate some good results. Repurposing of the polio vaccine would meet the immediate challenge of COVID-19. The next section of this paper discusses some scientific rationale behind the suggested use of the polio vaccine against COVID-19 (Figure 1).

FIGURE 1: SCIENTIFIC RATIONALE BEHIND THE SUGGESTIVE USE OF POLIO VACCINE AGAINST COVID-19



RATIONALE BEHIND THE SUGGESTED USE OF POLIO VACCINE AGAINST COVID-19

The similarity between Polio and SARS-CoV-2 virus: Both the SARS-CoV-2 and Poliovirus contain single-stranded positive-sense RNA (+ssRNA) as their genetic material. The Poliovirus consists of four coat proteins VP1, VP2, VP3, and VP4. There are sixty copies of each of these proteins that make the icosahedral protein shell of the Poliovirus. The genetic material of the Poliovirus is approximately 7500 nucleotides long having single-stranded positive-sense RNA (+ssRNA), encapsulated inside the icosahedral protein shell and makes a fully functional Poliovirus [23]. Similarly, SARS-CoV-2 is also made up of primarily four structural proteins namely, membrane glycoprotein (M), envelop protein (E), nucleo-capsid protein (N), and the spike protein (S) [24]. Both the viruses are invisible and unknown to the public, mostly asymptomatic but lethal too. The mode of transmission and spread of viruses is due to human to human contact; Poliovirus transmits through water contaminated with the fecal matter of infected person,

while transmission of SARS-CoV-2 is thought to be primarily by droplets [25].

Immunological determinants: A prompt and coordinated innate and adaptive immune response works as a first line of defense in SARS-CoV-2 infection. However, the excessive and uncontrolled immune response of the host immune system, such as cytokine storm, may be deleterious to the COVID-19 patient. The severity of COVID-19 pathology can be signified by a substantial surge in serum levels of pro-inflammatory cytokines (e.g., IL-1β, IL-2, IL-6, IL-8, IL-17, G-CSF, GM-CSF, IP-10, MCP-1, CCL3, and TNFa) as well as an absolute decline of circulating CD4+, CD8+, B cells and natural killer cells along with decreased levels of basophils, eosinophils, and monocytes [26]. In the case of Poliovirus infection, extraneural organ activation of IFNa/β in the CD155 transgenic mice model has been observed. Additionally, augmentation of cytokines and antigen presentation, as well as inhibition of NF-κB, has also been observed in post-poliovirus infection [27].

Several case studies at autopsy of the lung from people who died due to COVID-19, shows infiltration in alveolar immune cells. A post-mortem outcome from 38 patients who died due to COVID-19 showed plenty of CD68 positive macrophages present in the alveolar lumen and a few CD45 positive lymphocytes were seen in the interstitial space [26]. Another case study of histology of lung autopsy of a COVID-19 patinets indicated a low amount of polymorphonuclear neutrophils (PMN) and the moderate number of macrophages was present in the alveolar exudate, whereas infiltration of monocytes and T cells, but not B cells, was seen in interstitial compartment [28].

Clinical implications: Recent studies show Poliovirus vaccine can show cross-reactivity and thereby induce adaptive immunity and prevent the infection from SARS-CoV-2. Administration of Poliovirus vaccine generates antibodies against RdRP (RNA dependent RNA polymerases) protein, binds to RdRP of both Poliovirus as well as SARS-CoV-2 [14]. Another study that explored the effect of other available vaccines and their role in preventing SARS-CoV-2 infection shows that people administered with Polio vaccine show a lower rate of SARS-CoV-2 infection [29]. However, several vaccines have been developed for COVID-19, alternative therapeutical approaches, in addition to the repurposing of old drugs (as explained above), are needed to develop the potential drug against SARS-CoV-2 to contain the viral infection.

Most recent COVID-19 vaccination has the strongest nonspecific effects, therefore, we hypothesize that, even though SARS-CoV-2 suppresses TLR signaling, the prophylactic use of OPV or other LAV could activate innate immunity before COVID-19 infection via TLRs, priming the immune response/system for adaptive immunity if SARS-CoV-2 infection occurs later. Despite the UNICEF and WHO's efforts to phase down OPV a year after wild Poliovirus eradication, the potential advantages of OPV for COVID-19 need prospective research to determine the impact of OPV on COVID-19 illness and death globally. High rates of morbidity and death associated with COVID-19 have already seen globally [30], therefore, it is critical to do these trials as soon as possible.

CONCLUDING REMARKS

Significant vaccination is needed in society to achieve herd immunity against COVID-19. Some vaccines for COVID-19 have recieved emergency approval for use and some are under the development phase in different countries of the world. There is a large overall population of the world is to be vaccinated but many are hesitant with the currently used COVID-19 vaccines. The use of FDA approved Polio vaccine against COVID-19 is tested and safe, therefore, it could be thought of as one more option. Some common points are also associated between Polioviruse and SARS-CoV viz, their primary replication and possible cross-protective innate immunity offered by Polio vaccine further suggested it's repurposing for immune-prophylaxis and prevention of COVID-19. It will surely save time, resources, and lives of billions of people worldwide and protect society which is currently facing the COVID-19 pandemic.

DECLARATIONS

Ethics approval and consent to participate:

This article does not contain any studies involving human participants or animals performed by any of the authors.

Consent for publication:

Not applicable

Availability of data and material:

Not applicable

Competing interests:

None

Funding:

The authors have no financing to disclose.

Acknowledgements:

Authors are grateful to the National Institute of Technology, Raipur (CG), India and Shri Ramswaroop Memorial University (SRMU), Barabanki (UP), India for providing the facility and space for this work.

All authors have read and approved the manuscript

References

1. Soltani S, Zakeri A, Zandi M, Kesheh MM, Tabibzadeh A, Dastranj M, Faramarzi S, Didehdar M, Hafezi H, Hosseini P. The role of bacterial and fungal human respiratory microbiota in COVID-19 patients. BioMed Research Intl. 2021; https://doi.org/10.1155/2021/6670798
2. Talento AF, Hoenigl M. Fungal infections complicating COVID-19: with the rain comes the spores. J. Fungi. 2020; 6:279.
3. Chowdhary A, Sharma A. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect the company public news and information. 2020.
4. Rawson TM, Wilson RC, Holmes A. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19. The COVID-19 resource centre is hosted on Elsevier Connect, the company ' s public news and information. 2020.
5. Arastehfar A, Carvalho A, Nguyen MH, Hedayati MT, Netea MG, Perlin DS, Hoenigl M. COVID-19-associated candidiasis (CAC): an underestimated complication in the absence of immunological predispositions? J. Fungi. 2020; 6:211-223.
6. Kubin CJ, McConville TH, Dietz D, Zucker J, May M, Nelson B, Istorico E, Bartram L, Small-Saunders J, Sobieszczyk ME. Characterization of bacterial and fungal Infections in hospitalized patients with Coronavirus Disease 2019 and factors associated with health Care-Associated Infections. Open Forum Infect. Dis. 2021; 8. https://doi.org/10.1093/ofid/ofab201
7. Blok BA, Arts RJ, van Crevel R, Benn CS, Netea MG. Trained innate immunity as underlying mechanism for the long-term, nonspecific effects of vaccines. J Leukoc Biol 2015; 98: 347-356.
8. De Bree LC, Koeken VA, Joosten LA, Aaby P, Benn CS, van Crevel R. Non-specific effects of vaccines: Current evidence and potential implications. Semin Immunol. 2018; 39: 35-43.
9. Higgins JP, Soares-Weiser K, Reingold A. Systematic Review of the Non-specific Effects of BCG, DTP and Measles Containing Vaccines. Geneva: World Health Organization. 2014.
10. Jensen KJ, Benn CS, van Crevel R. Unravelling the nature of non-specific effects of vaccines a challenge for innate immunologists. Semin Immunol. 2016; 28: 377-383.
11. Aaby P, Benn CS. Beneficial nonspecific effects of oral polio vaccine (OPV): Implications for the cessation of OPV? Clin Infect Dis. 2017; 65: 420-421.
12. Higgins JP, Soares-Weiser K, López-López JA, Kakourou A, Chaplin K, Christensen H. Association of BCG, DTP, and measles containing vaccines with childhood mortality: Systematic review. BMJ. 2016; 355:i5170. doi: 10.1136/bmj.i5170.
13. Upfill-Brown, A, Taniuchi M, Platts-Mills JA, Kirkpatrick B, Burgess SL, Oberste MS. Nonspecific effects of oral polio vaccine on diarrheal burden and etiology among Bangladeshi infants. Clin Infect Dis. 2017; 65: 414-419.
14. Pawlowski C, Puranik A, Bandi H, Venkatakrishnan AJ, Agarwal V, Kennedy R. Exploratory analysis of immunization records highlights decreased SARS-CoV-2 rates in individuals with recent non-COVID-19 vaccinations. Sci Rep. 2021; 11(1):4741. doi: 10.1038/s41598-021-83641-y.
15. Thevar S. More children COVID positive in second wave. Hindustan Times. 2021; Available. https://www.hindustantimes.com/cities/pune-news/more-children-covid- positive-in-second-wave-101618657160956.html
16. Abd El-Aziz TM, Stockand JD. Recent progress and challenges in drug development against COVID-19 coronavirus (SARS-CoV-2)-an update on the status. Infect Genet Evol. 2020; 83:104327. doi:10.1016/j.meegid.2020.104327.
17. Pushpakom S, Iorio F, Eyers P. Drug repurposing: progress, challenges and recommendations. Nat Rev Drug Discov. 2019; 18, 41–58.
18. Lloyd T. A Phase 3 randomized double blind efficacy and safety study of oral Polio Vaccine and NA-831 for Covid-19 (OPV-NA831). Available

<https://clinicaltrials.gov/ct2/show/NCT04540185> (9/9/2022).

19. Sandhya R. 100-year-old TB vaccine now being tested for Covid-19, India may conduct a trial too. 2020 Available <https://theprint.in/health/100-year-old-tb-vaccine-now-being-tested-for-covid-19-india-may-conduct-a-trial-too/387839/> (25/3/2020).
20. Gautret P. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents. 2020; 20:105949.
21. Zhou Y. Network-based drug repurposing for novel coronavirus 2019-nCoV/SARS-CoV-2. Cell Discov. 2020; 16; 6:14.
22. Cao B, Yeming W. et al. A Trial of Lopinavir Ritonavir in adults hospitalized with severe COVID-19. N Engl J Med. 2020; 382: 1787-1799.
23. Wein MW, Chow M, Hogle JM. Poliovirus: new insights from an old paradigm. Structure 1996; 4:763-767.
24. Hu B, Guo H, Zhou P. et al. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol. 2021; 19: 141-154.
25. Shurtleff D. Polio and COVID-19. 2020; https://wcaap.org/polio-and-covid-19/ .
26. Catanzaro M, Fagiani F, Racchi M. Immune response in COVID-19: addressing a pharmacological challenge by targeting pathways triggered by SARS-CoV-2. Sig Transduct Target Ther. 2020; 5, 84; https://doi.org/10.1038/s41392-020-0191-1
27. Aguiar D, Lobrinus JA, Schibler M, Fracasso T, Lardi C. Inside the lungs of COVID-19 disease. Int J Legal Med. 2020;134:1271-1274.
28. Carsana L, Sonzogni A, Nasr A, Rossi RS, Pellegrinelli A, Zerbi P, Rech R, Colombo R, Antinori S, Corbellino M, Galli M, Catena E, Tosoni A, Gianatti A, Nebuloni M. Pulmonary post-mortem findings in a large series of COVID-19 cases from Northern Italy. Lancet Infect Dis. 2020; 20:1135-1140.
29. Sun Y, Abriola L, Niederer RO, Pedersen SF, Alfajaro MM, Monteiro VS, Wilen CB, Ho YC, Gilbert WV, Surovtseva YV, Lindenbach BD, Guo JU. Restriction of SARS-CoV-2 replication by targeting programmed −1 ribosomal frameshifting. Proc Natl Acad Sci USA 2021, 118(26):e2023051118.
30. Kumar, A. COVID-19 gripped the globe with some unnoticed facts and too many questions. VirusDis. 2021; 32: 609–612.