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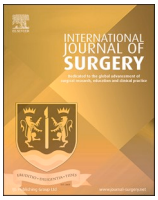
International Journal of Surgery 107 (2022) 106971

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu



Correspondence

FDA's authorized "JYNNEOS" vaccine for counteracting monkeypox global public health emergency; an update – Correspondence

Dear Editor,

The recently re-emerging outbreaks of monkeypox (MPX), caused by monkeypox virus (MPXV) have once again drawn global attention to this illness due to its unexpected sudden rise in cases in several non-endemic countries beyond Africa. As a Public Health Emergency of International Concern (PHEIC), currently 53,027 confirmed cases and 15 deaths have been reported from 100 countries and locations up to September 5, 2022, and the rapid rise in MPX cases from May 2022 onwards reflects more and more cases to be seen in coming time, and concern has been raised by a few researchers whether this looming PHEC could pose another pandemic amid the ongoing COPVID-19 pandemic? [1,2]. The MPXV belongs to the Poxviridae family, genus Orthopoxvirus, the same genus as of variola virus, which causes smallpox. To date, no definite treatment exists for the disease, but smallpox immunizations have helped to contain MPX outbreaks due to cross-immunity protection of persons who received smallpox vaccinations [3]. However, due to cessation of smallpox vaccination after its eradication in 1980, increasing infection with MPXV, particularly in younger population (less than 40–50 years) who were not vaccinated eventually, and consequently now the MPXV has emerged as the most important Orthopoxvirus posing high public health concern [4,5]. The results indicated that previous protection against smallpox vaccine resulted in roughly 85% protection against MPX [6]. JYNNEOS and ACAM2000 are the two smallpox vaccines that the Food and Drug Administration (FDA) has currently licensed for use in the prevention of monkeypox [3,7]. This correspondence article highlights the significance of JYNNEOS vaccine in rendering protection for prevention and control of current MPX outbreaks, some vaccine associated side effects that need to be taken care of and more clinical research and vaccination data need to be explored for optimizing its real value to fight against the PHEC, and to alleviate any feasible pandemic situation by promoting its administration till specific vaccine is developed against monkeypox.

According to a recent opinion, MPX has a clinical appearance similar to smallpox with initial flu-like symptoms such as fever, chills, headache, exhaustion, and muscle aches as well as an additional distinctive symptom of lymphadenopathy. A centrifugally spread maculopapular rash appears after a febrile prodrome. Crusts can remain attached for up to four weeks before a new layer of skin forms and the illness clears up [3,4]. The latest view also mentioned sexual contact, respiratory droplets from infected individuals, and direct contact with infectious sores or scabs as probable routes for virus transmission. The virus was initially identified in 1958, and its first case in human was recognized in the 1970 as a zoonotic infection, and problems with its diagnosis and prevention still exist after more than five decades in places of extreme poverty [3,8]. The secondary attack rate for unprotected household contacts of patients with MPXV disease was 9.28% in the research conducted in the Democratic Republic of Congo in the late 1980s, while it was only 1.31% for vaccinated contacts.

Given the rapid global spread of MPX, the availability of effective vaccines, and the unknown risk-benefit profile of current antivirals, immunization will likely be a crucial technique for controlling MPX in humans. Vaccination should be prioritized for those at highest risk, including children, those with impaired immune systems, and healthcare personnel at high risks of occupational exposure. Pre-exposure vaccination, post-exposure prophylaxis, and ring vaccination of close contacts are all possible immunization techniques [9,10].

The Centers for Disease Control and Prevention (CDC), in preparation for potential public health emergencies, contracted for the creation of ACAM2000 vaccine, which is made from a live replication-competent Vaccinia virus [11,12]. As of August 31, 2007, those at elevated risks of contracting smallpox were allowed to use the ACAM2000 vaccination after receiving approval from the FDA. This replication-competent virus vaccine has the ability to escape from the injection site and propagate to other areas of the body and to other people. As a result, until the vaccine site is fully healed, which usually takes four weeks, it must be properly cared for in vaccinated persons. Clinical investigations that revealed myopericarditis occurred at a rate of 5730 per million (seven instances in 1307 individuals) in recipients of this vaccine demonstrated that ACAM2000 carries several additional dangers like progressive vaccinia and eczema vaccinatum. Along with encephalitis, encephalomyelitis, and encephalopathy, other serious side effects of this vaccine include ocular problems, blindness, and encephalopathy. Death of unvaccinated individuals who had contact with vaccinated individuals was also observed [7,11,12].

A different vaccine called JYNNEOS (also known as Imvamune and Imvanex) is presently licensed in the United States to prevent smallpox, according to the CDC Monkeypox and Smallpox Vaccine Guidance which was revised on June 2, 2022. The recommendation further noted that this vaccine, unlike ACAM2000, is a non-replicating modified Vaccinia Ankara virus vaccine and it is given as a subcutaneous injection of 0.5 ml, in two doses separated by a gap of 28 days. The CDC also said in its instructions that there is no chance of the live virus spreading to other persons or other parts of the body because it cannot shed from the injection site. Unlike ACAM2000, which can cause live virus generation in vaccinated patients, JYNNEOS does not, and hence it is safer for usage in immunocompromised individuals. Protection from the JYNNEOS vaccination may be weaker in immunocompromised persons since their immune systems are not as strong as those of healthy people. Injection site reactions, throat tightness, myalgia, headache, chills, and nausea are the most frequently reported side effects of JYNNEOS in clinical trials. Protection from smallpox is determined by whether a "take" (the formation of intradermal scarification, resulting in a severe cutaneous

https://doi.org/10.1016/j.ijsu.2022.106971
Received 7 September 2022; Accepted 26 October 2022
Available online 29 October 2022

reaction "pustule" at the vaccination site) has occurred. Since JYNNEOS cannot replicate in human cells, it does not cause severe cutaneous reactions [13].

The Advisory Committee on Immunization Practices (ACIP) voted in favor of JYNNEOS as a substitute for ACAM2000 for immunizing those at risk of contracting the orthopoxvirus on November 3, 2021 [12,14]. The FDA granted a JYNNEOS vaccine emergency use authorization (EUA) in August 2022, enabling medical professionals to administer the shot subcutaneously to patients under the age of eighteen and intradermally to those who are 18 years of age or older [15]. Prophylaxis against MPXV after exposure is achieved with this vaccination. The CDC suggests giving the vaccination as post-exposure prophylaxis to anyone in the intermediate- or high-risk categories (unprotected contact with the body fluid of infected person or contact with less than 6-m distance with the infected person). Countries like Canada, Europe, and Britain have JYNNEOS vaccines available for their citizens [16].

JYNNEOS and IMVAMUNE, two brands of modified vaccine ankara (MVA), can be given subcutaneously and intradermally. The intradermal approach uses 80% less antigen than the oral route, which can boost the dose availability by five times and make it easier to vaccinate a broad population, according to a 2015 study that compared the two administration routes. Although treatment via the intradermal method results in redness, irritation, and stiffness, these adverse effects are tolerable [17]. For those with HIV or atopic dermatitis, the vaccination has been confirmed to be safe [18].

Although JYNNEOS appears to be a safer option for the present monkeypox outbreak, much remains unknown regarding the vaccine's efficacy and durability. The vaccine is about 85% effective, according to data from prior studies [12], but more research is needed to validate its current efficiency because the data is slowly ageing and has to be updated. Since many medical professionals have expressed concerns about the immunity provided by JYNNEOS, more research is needed to determine how long-lasting the effects of immunity provided by the two-dose vaccination are in order to make recommendations regarding the frequency of booster the doses. Trials have demonstrated that ACAM2000 entails a number of dangers, while there is little data to support the similar claim for JYNNEOS. Therefore, more investigation is essential to update both. The position of ACAM2000 as a safe immunization therapy and experiments should be conducted to determine whether administration of JYNNEOS has hazards similar to those associated with other pox vaccines or not. Another significant issue that deserves attention is the requirement to assess the safety and effectiveness of this replication-deficient vaccination in breast-feeding women. Trials should be conducted to determine JYNNEOS′ impact on lactating women to determine whether JYNNEOS is released in human milk to aid in giving infants passive immunity [14].

In light of the current rapid global spread of MPX, the availability of effective vaccinations, and the unknown risk-benefit profile of current antivirals, immunization will likely to be a crucial method for minimizing MPX cases in humans. Healthcare professionals at considerable risk of occupational exposure to MPXV, patients with impaired immune systems, and youngsters should be vaccinated first. Post-exposure vaccination, vaccinating close contacts, and non-pharmaceutical barriers can all be utilized to reduce the likelihood of an outbreak among humans [7,10]. The World Health Organization (WHO) has said that mass vaccinations are unnecessary and that vaccination decisions should be made after carefully weighing the risks and benefits in each individual case of MPX [5].

More research is needed to discover how long immunity lasts with JYNNEOS vaccination after receiving the 2-doses, at which point recommendations of the frequency of booster doses can be adjusted. If exposures to orthopoxviruses occur before peak immunogenicity is achieved, the efficacy of a single dose JYNNEOS should be assessed [19]. To evaluate the risks and provide advice concerning co-administration of JYNNEOS with mRNA COVID-19 vaccinations, clinical trials examining the risk for myopericarditis, and significant side events are necessary. Confirming successful immunization in certain populations and learning more about the efficacy of a single dose of the JYNNEOS vaccine could benefit from the establishment of a correlate of protection following vaccination. Additionally, extensive studies are lacking to identify the specific reservoir of othopoxvirus (such as monkeypox virus); knowing specific reservoir helps to understand the different properties of the virus and the high-risk behaviors for acquiring orthopoxvirus infections.

In conclusion, the FDA's approval of JYNNEOS for use as an emergency vaccination is a major start toward containing the current monkeypox outbreaks posing global health emergency, but more research is required to establish JYNNEOS as a reliable alternative to previously used live-replicating vaccines. Conclusive trials are necessary to demonstrate the benefits of administering this vaccine, taking into account the risks it poses and contraindications to using it. Recent worldwide epidemics have once again emphasized the significance of maintaining a vigilant watch, enhancing surveillance, and formulating innovative preventative and treatment approaches along with proactive control measures to be implemented timely to limit the spread of re-emerging viruses posing global public health emergency such as MPXV, which was earlier considered to be a neglected or rare disease (MPX). There is yet time with us to develop an effective and safe new generation vaccine, for which high efforts are now being made that could counteract the virus before it could be feasibly be labeled to pose another pandemic situation amid the ongoing COVID-19 pandemic.

Ethical approval

Not applicable

Sources of funding

No funding received.

Author contribution

Ranjit Sah, Mahnoor Humayun and Eesha Baig wrote the manuscript. Huzaifa Ghulam Hussain, Usama Shahid conducted the literature search. Minaam Farooq, Huzaifa Cheema, Deepak Chandran, Mohd. Iqbal Yatoo Anil K. Sharmad and Kuldeep Dhama supervised the project, edit the manuscript. All authors read and approved for the final manuscript.

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. Please note that providing a guarantor is compulsory.

Ranjit Sah.

Data statement

All data included in the manuscript.

Provenance and peer review

Not commissioned, internally peer-reviewed.

Declaration of competing interest

No conflicts of interest.

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Ranjit Sah[*,1]
Harvard Medical School, Boston, USA
Tribhuvan University Teaching Hospital, Institute of Medicine, Kathmandu, Nepal

Mahnoor Humayun[1]
Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan
E-mail address: mahnoorhumayun9@gmail.com.

Eesha Baig
Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan
E-mail address: eeshabaig15@gmail.com.

Minaam Farooq
Department of Medicine, King Edward Medical University, Mayo Hospital, Lahore, Pakistan
E-mail address: minaamkemu2018@gmail.com.

Huzaifa Ghulam Hussain
Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan
E-mail address: Huzaifa.ghulamhussain@gmail.com.

Muhammad Usama Shahid
Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan
E-mail address: Usamashahidkhan123@gmail.com.

Huzaifa Ahmad Cheema
Department of Medicine, King Edward Medical University, Mayo Hospital, Lahore, Pakistan
E-mail address: huzaifaahmadcheema@gmail.com.

Deepak Chandran
Department of Veterinary Sciences and Animal Husbandry, Amrita School of Agricultural Sciences, Amrita Vishwa Vidyapeetham University, Coimbatore, 642109, Tamil Nadu, India
E-mail address: c_deepak@cb.amrita.edu.

Mohd Iqbal Yatoo
Division of Veterinary Clinical Complex, Faculty of Veterinary Sciences and Animal Husbandry, Sher-E-Kashmir University of Agricultural Sciences and Technology of Kashmir, Shalimar, Shuhama, Alusteng, SrinagarSrinagar, 190006, Jammu and Kashmir, India
E-mail address: iqbalyatoo@gmail.com.

Anil K. Sharma
Department of Biotechnology, Maharishi Markandeshwar University (Deemed to be University), Mullana, Ambala, 133207, Haryana, India
E-mail address: anibiotech18@gmail.com.

Kuldeep Dhama
Division of Pathology, ICAR-Indian Veterinary Research Institute, Bareilly, Izatnagar, Uttar Pradesh, 243122, India
E-mail address: kdhama@rediffmail.com.

[*] Corresponding author. Infectious Diseases Fellowship, Clinical Research (Harvard Medical School), Global Clinical Scholars Research Training (Harvard Medical School), 44600, Kathmandu, Nepal.

E-mail addresses: ranjitsah@iom.edu.np, ranjitsah57@gmail.com (R. Sah).

[1] Both authors contributed equally.