Monkeypox breakthrough infections and side-effects: Clarion call for nex-gen novel vaccine

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Dear Editor,

Monkeypox (mpox) virus belongs to the same family as variola virus causing smallpox. Usually spreading through skin-to-skin contact with the mpox-infected and causing rashes, this viral disease remained neglected before the recent (2022) outbreak. Although severity of the illness is high in the immunocompromised, the pregnant and the children, most of the infected recover in few weeks. However, the current mpox outbreak seems mysterious. The 2022 mpox transmission is associated with sexual contacts almost exclusively affecting the sexually active gay, bisexuals and men having sex with other men [1]. The mpox cases among women and non-binary individuals are also observed [1]. The US has approved two vaccinia-derived mpox vaccines as preventives. These are replication-deficient modified vaccinia Ankara (MVA) vaccine JYNNEOS™ (Imvamune or Imvanex), and replication-competent vaccinia virus vaccine ACAM2000® [2].

JYNNEOS (Imvamune or Imvanex) is a live, nonreplicating MVA vaccine and is preferred for the current mpox outbreak as it is relatively safe. It is approved as a two-dose series to prevent smallpox and mpox in people above 18 years. USFDA authorised emergency use of JYNNEOS™ in people below 18 years to facilitate curb mpox. One will need to receive two doses of the vaccine at least 28 days apart for full vaccination. Best protection against mpox is ensured two weeks after the second vaccine dose. ACAM2000® is a live replication-competent vaccinia virus vaccine approved for mpox which has greater risk with certain serious side-effects, and should not be administered to people with weak immune systems, certain skin conditions like eczema, heart ailments, or the breastfeeding, pregnant or thinks she is pregnant. Although it may not cause mpox or smallpox, it may cause clinical vaccinia infection among humans with transmission potential. The CDC recommends ACAM2000® only as an alternative to JYNNEOS™ for infants (of 1 year age) and older that are at high mpox infection risk. The common side-effects of both the vaccines are injection-site reactions, headache, muscle pain, fever, chills, fatigue, nausea and altered appetite.

JYNNEOS™ dose is not recommended for people with serious health issues (like severe allergic reaction to previous dose of JYNNEOS™, gentamicin, ciprofloxacin, or to chicken or egg protein). Although rare, such cases are life-threatening with symptoms including hives, difficulty in breathing, dizziness, fast heartbeat, swelling of the face and throat [2]. Common reported side-effects of ACAM2000® vaccination are fever, headache, fatigue, body-ache, sore arm, itching, swollen lymph nodes and mild rash. Serious side-effects like swelling of the brain or spinal cord, myocarditis and pericarditis, blindness and severe allergic reactions are also reported [2]. People with HIV, high blood pressure, high cholesterol, high blood sugar, diabetes, heart or blood vessel problems, skin problems, and allergic to antibiotics like neomycin and polymyxin B and infants

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younger than 12 months are at greater risk if they receive ACAM2000® [2]. The CDC recommends JYNNEOS™ as the primary vaccine due to fewer potential side-effects compared to ACAM2000® [2].

Hazra et al. (2022) reported mpox infection at the mpox testing and vaccination site after MVA-BN vaccine dosing [3]. They observed two breakthrough infections at least 3 weeks after the second dose. As mpox incubation ranges from 5 to 21 days, an observation that is worth mentioning here is that, the cases occurring between 1 and 14 days after vaccination may not represent true vaccine failure [3,4]. There is a possibility of an earlier exposure and such vaccine recipients may have sought for it after realising that they were mpox exposed. The study has limitations like, a small number of recipients, and a non-uniform observation period after the vaccination across the cohort. To understand the vaccine efficacy and the duration of the immune response, studies at greater scales are therefore recommended. Immunogenicity data suggest robust response rates (100% at 2 weeks) after the second vaccine dose [5]. The data on the efficacy in clinical use are limited due to limited MVA-BN availability. Owing to its low current supply, the local health authorities have resorted to single-dose and low-volume dosage strategies to maximise vaccine availability.

Potential breakthrough infections were evaluated in recipients of JYNNEOS™ (Imvanex) vaccine with high-risk mpox exposure [5]. A total of 276 participants received single dose of the vaccine 11 days after mpox exposure. Mpox infection developed in 12 recipients, of which 10 recipients manifested it in 5 days, 1 in 22 days, and 1 in 25 days after vaccination. However, no severe adverse events or safety concerns were noticed. The recipients that did not develop mpox infection received the second dose after 29-day median. The two participants that manifested breakthrough infections by the 22nd and 25th day had a pet (cat and dog) at home, both the pets although were asymptomatic. However, important limitations of the study were, it was carried out at a single center, the mpox exposure was not assessed, and the study did not consider a control group or measures of vaccine-elicited immunity.

No verifiable data on the efficacy of JYNNEOS™ or ACAM2000® against mpox is available yet. In view of this till many aspects of concern are revealed, people getting vaccinated are highly recommended to continue with measures to protect themselves from infection by avoiding close and intimate contacts. No vaccine could ever provide a 100% foolproof protection. Although the overall efficacy of mpox vaccine is unclear, one aspect is clear that the vaccine dose stimulates the immune system and elicits antibody production. To determine its efficacy in the ongoing outbreak better, an open call for international studies on mpox vaccine is urgently contemplated. Although there is a global decline in mpox cases, however it is too early to conclude that the vaccine has primarily contributed to it. As breakthrough infections post the mpox vaccination are reportedly occurring and the mpox virus allegedly continuously mutate, strict precautions are essential to reduce its spread. Mutations like M17411, D209 N and P722S located in B21R surface glycoprotein are linked to the immune-evasion [5]. Considering mutations, the vaccine side effects and breakthrough infections, developing a mutant-proof, nex-gen vaccine for mpox virus that may be more effective and safe is recommended.

Author's contributions

All the authors contributed significantly in developing the manuscript. RKM: conceptualised the manuscript and wrote the first draft with input from AAR, SM, AM, BKP, RS: updated, reviewed and edited the manuscript. All the authors have reviewed and approved the final draft for submission.

Data availability statement

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Declaration of competing interest

There is no potential conflict of interest.

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