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Original Article

Protective immunity rate against monkeypox: expectation for present and future in case that there is no smallpox vaccine booster

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Abstract: Objectives: Monkeypox is now regarded as a major global public health concern. A common symptom of this disease is an acute febrile illness with skin sores. The likelihood of the virus spreading from person to person is increasing. The aim of the present study is to estimate the protective immunity rate against monkeypox. Methods: Based on the current situation in Africa, the authors forecast the protective immunity rate against monkeypox for the present and future if a smallpox vaccination booster is not available. The clinical mathematical model was used. The primary data for analysis include data on the current serological rate against smallpox and data on the declining rate of smallpox immunity after the last vaccination. Results: According to the current clinical modeling study, protective immunity to monkeypox is limited. The rate among people who have previously been immunized against smallpox is still higher than the general population rate. If the present monkeypox outbreak (2022) is not successfully controlled, there could be a severe public health danger, such as a pandemic. On a larger scale, in a few years, no immunity will be a concern. Conclusions: To suppress the current monkeypox outbreak, it may be necessary to research the use of a novel monkeypox immunization or a traditional smallpox vaccine.

Keywords: Serology, immune, monkeypox, smallpox, vaccine

Introduction

Orthopoxviruses, parapoxviruses, and yatapoxviruses are three genera of the Poxviridae family that have been linked to human zoonoses [1]. The majority of cases are work-related, sporadic, have minimal cutaneous lesions, and have modest morbidity [1]. Monkeypox, on the other hand, has a high morbidity and mortality rate comparable to smallpox [1]. Monkeypox and cowpox viruses are regarded as emerging at this time; their high risk of spread is a result of increased worldwide travel, trends for new animals as pets, and the loss of smallpox vaccination protection [2]. As the most significant orthopoxvirus infection in humans in the smallpox post-eradication era, monkeypox is an emerging zoonotic disease. Monkey pox has a clinical appearance that is comparable to smallpox [3]. The risk of the virus transferring from one person to another is increasing [4]. Understanding the disease is critical since early diagnosis and suitable therapy are required for effective disease treatment. Routine laboratory tests, such as a complete blood count, cannot provide a conclusive diagnosis of monkeypox [2]. The current diagnostic standard for monkeypox is the molecular diagnosis of the virus in collected clinical samples from patients' lesions [2]. On the other hand, neither a fever nor a skin lesion is common [4]. In 2022, numerous non-endemic countries saw an outbreak of human monkeypox. According to the World Health Organization (WHO), this outbreak is "atypical" [13-20]. So far, reported instances have primarily, but not solely, been detected among gay and bisexual men aged 20 to 50. It's crucial to keep in mind that certain people, such as those who have neurological or digestive problems, only exhibit particular symptoms [5-7]. The concept of universal prevention is one of the major barriers to overcoming this new public health issue. More research is needed in order to properly combat the monkeypox outbreak. However, traditional illness prevention measures are effective and useful.

Vaccination is a possible primary preventive measure against the emerging monkeypox [8].

Vaccines against JYNNEOSTM (live, replication incompetent vaccinia virus) and ACAM2000® (live, replication competent vaccinia virus) are already on the market [9]. It is not, however, currently included in any country's routine vaccination regimen [9]. The question of smallpox immunization's cross-protective impact is intriguing. Previous studies discovered that the smallpox vaccine, which had previously been withdrawn in 1980, provided approximately 85% protection against monkeypox [10]. There has been an increase in monkeypox cases, particularly in the highly endemic areas, as well as a spread to neighboring countries and a shift in the median age from young children to young adults [11]. These findings could be linked to the discontinuation of smallpox immunization, which offered some cross-protection against monkeypox and resulted in greater human-to-human transmission. The emergence of outbreaks outside of Africa emphasizes the disease's global significance [10]. After decades of no smallpox vaccination, there is a significant decrease in the protective immunity rate against monkeypox. Increased surveillance and detection of monkeypox cases are critical tools for understanding the disease's ever-changing epidemiology [11]. The public health clinical immunology focus in the present monkeypox outbreak is on the population's overall protective immunity. The serological immune level against monkeypox is an interesting issue to be studied.

The authors give an expectation on serological immunity levels against monkeypox for the present and future in the absence of a booster dose of the smallpox vaccination based on the existing scenario in Africa.

Materials and methods

Study design

This is a clinical mathematical model study. The relevant data was subjected to a retrospective descriptive analysis. The epidemiological surveillance data in the African endemic area of monkeypox were reassessed. A database search was initially undertaken to get data for inclusion. The standard database was chosen as PubMED (www.pubmed.com). "Monkeypox", "reemergence", and "Africa" are some of the search terms. Only valid published data from PubMED, a global reference database, was used. Exclusion is used when there is missing or incomplete data. In the primary search, 17 publications were discovered (data as of July 2022). For further research, only the article including complete data on the incidence of monkeypox in endemic parts of Africa at various dates following the termination of smallpox immunization was included. Exclusion was set in any document without complete data. For further mathematical model study, only documents with data on the current serological rate against smallpox or the declining rate of smallpox immunity after the last vaccination are included.

Mathematical modeling

To generate the clinical mathematical model, the primary data are: a) data on the current serological rate against smallpox, b) data on the declining rate of smallpox immunity after the last vaccination. The primary assumption is that smallpox immunity after a complete vaccination is equal to 100% and declines over time. The rate of decline, according to the previous publication, is equal to 1.29% per year [12]. The basic data for the protection rate against smallpox among the general population in an African country is available in the study by Nguyen et al [12]. According to that study, which represented the data in 2021, only 10.1% of the total population was vaccinated against smallpox; the serologic immunity level was 25.7% among vaccinated people and 2.6% in the overall population [12]. These data are typically assigned as the starting point for modeling.

The mathematical model is used to calculate the projected serologic immunity rate against monkeypox in the local population. Gradual manipulation is used to get the desired result. First, the level of protective immunity against monkeypox is evaluated. Based on a report, the smallpox vaccine can provide around 85% protection against monkeypox [10]. As a result, the anticipated protective immunity rate for monkeypox will be "0.85 times theprotective immunity rate for smallpox at its starting point." The second phase is to forecast the predicted future serologic immunity rate in the absence of smallpox vaccine boosters. The previously

Table 1. The expected protective immunity rates for monkeypox at different future period if there is no smallpox vaccine boostering

Periods	Expected protective immunity rates (%)	
	Vaccinated persons	Overall population
2021	21.9	2.2
2022	20.6	0.9
2023	19.3	0
2024	18.0	0
2025	16.7	0
2026	15.5	0
2027	14.2	0
2028	12.9	0
2029	11.6	0
2030	10.3	0

reported diminishing immunity rate of 1.29% per year can be used to make the prediction. The indicated rate is utilized as a factor in continuous serial subtraction to calculate the projected protective immunity rate at various future times. The described mathematical model can be used to estimate the protective immunity rate at different periods in the future. The model can be simply operated using a standard arithmetic calculation. There is no interference from biological factors because the model uses a strictly mathematical methodology.

Statistical analysis

Because this is a descriptive study, there is no comparison group and there is no analytical statistical analysis. The basic principle of arithmetical manipulation is used, and the triangular law is applied.

Ethical issue

This is a pure clinical informatics study, and it is exempt from ethical committee approval. There is no human, animal or clinical specimen sample included and informed consent is not applicable.

Results

Starting expected protective immunity rate for monkeypox

Using the earlier mentioned modeling technique, the expected protective immunity rate for monkeypox can be calculated according to this equation: "starting expected protective immunity rate for monkeypox = starting expected protective immunity rate for smallpox x 0.85". According to the calculation, the serologic immunity levels are equal to 21.9% among vaccinated people and 2.2% in the overall population.

The future expected serologic immunity rate for monkeypox

Applying the declining factor over time, the expected protective immunity rates for monkeypox at different future periods if there is no smallpox vaccine booster are shown in **Table 1**. According to serial analysis, at the 18th and 3rd years, there will be no protective immunity rate among vaccinated people and the general population.

Discussion

Monkeypox is now regarded as a major global public health concern [13-20]. A common symptom is an acute febrile illness with skin lesions [4]. The likelihood of the virus spreading from person to person is increasing [4]. Monkeypox is transmitted to humans through contact with or consumption of an infected animal, as well as direct contact with the natural host's blood and body fluids [17]. Recent studies on human scenarios, including sexual intercourse, highlight the most pressing contemporary concerns. The latest monkeypox outbreak raises concerns that poxviridae have a high potential for zoonotic spread and pandemic. During earlier human outbreaks, healthcare and public health workers in Africa conducted extensive fieldwork and studies, and their experience should improve our worldwide response to the present outbreak [20]. However, unexpected clinical manifestations may now have significance in illness recognition [20]. Poxviridae infections, such as monkeypox, have common cutaneous symptoms that appear early, may be associated with periods of transmissibility, and can leave scars. As a result, dermatologists will be crucial in spotting and diagnosing infections [20]. Treatment should be considered for people with severe diseases, pregnant women, or children [2]. Tecovirimat is a proposed antiviral drug for the management of the case. However, there is limited data on the clinical efficacy of the new drug in therapy for monkeypox. Monkeypox can self-limit, and the prog-

nosis is typically good, regardless of the antiviral medication therapy.

Following the global elimination of smallpox in the 1970s, occurrences of monkeypox garnered international attention. The smallpox vaccine conferred immunity against the monkeypox virus. Monkeypox cases increased after the provision of the smallpox vaccine was discontinued [13]. It wasn't until the 2003 US outbreak that monkeypox received widespread attention [13]. Despite the moniker "monkeypox," the virus did not originate in monkeys. Several rodents and small mammals have been identified as the virus's origins; nevertheless, the true origin of monkeypox is unknown [13]. The exotic animal trade and international travel, combined with increased human sensitivity as a result of missed vaccinations, aided in the spread of the monkeypox virus to new locations [16]. The present outbreak, which has more than 10,000 cases in more than 50 countries between May and July 2022, demonstrates that the virus can move rapidly between people and hence pose a serious threat to public health with global implications [16].

Similar to other infections, protective immunity to monkeypox plays a role in disease prevention. Data from serological surveillance studies can show the status of protective immunity against the disease among the general population. If the serological data show that very few parts of the population have protective immunity against the disease, the risk of widespread infection in the event that an outbreak occurs is possible. The clinical significance of the serological data is the suggested indicator for public health planning against the disease. The authors of the current study used an informatics study to assess the protective immunity rate against monkeypox: current and future expectations in the absence of a smallpox vaccine booster. The confounding condition can be controlled because it is a modeling study. The current study clearly demonstrates the changing pattern of the protective immunity rate for monkeypox. Historically and currently, monkeypox prevention is reliant on the side benefit of widespread smallpox immunization. However, the serologic pattern for monkeypox may vary because smallpox has already been eradicated and no widespread immunization is advised.

Based on the authors' view, the current report can give useful data regarding the current status of protective immunity against monkeypox. The current clinical modeling study demonstrates that protective immunity to monkeypox is minimal. This means most people have no protection against the disease, and they are at risk of getting the infection in the current stage of re-emergence of the monkey pox. Of interest, the protective immunity rate among the smallpox-vaccinated cases is also low. Therefore, it is no doubt that the previously smallpox-vaccinated person might have a chance to get monkeypox. A recent report on monkeypox cases in smallpox-vaccinated people is an excellent example [21]. Nevertheless, the protective immunity rate among those who have previously had smallpox immunization is still greater than the general population rate. However, on a larger scale, there will be an issue of no immunity within a few years, and if the current monkeypox outbreak (2022) cannot be properly handled, there may be a major public health problem, such as a pandemic. It may be time to investigate employing a novel monkeypox vaccination or a conventional smallpox vaccine to control the present monkeypox outbreak. Based on the current expectation, within a few years in the future, the protective immunity will turn near zero, and it should be time to reconsider a mass vaccination requirement.

Regarding the shortcoming of the present study, due to the nature of a model study, the background condition is fixed, and if there is a new changing condition such as mutation, the situation might deviate from the model. It should be a global concern to design an effective vaccine against the spreading monkeypox problem, though, given the possibility of several additional elements that could lead to a more severe situation of a monkeypox epidemic.

Conclusion

At present and in the future, the predictive study can show that the protective immunity for monkeypox is low. The rate among people with previous smallpox vaccinations is still higher than the average level for the general population. However, on a general population scale, there will be a problem of no immunity within a few years, and if the outbreak of monkeypox at present (2022) cannot be successfully con-

tained, there might be a big public health problem such as a pandemic. It may be time to think about employing the novel monkeypox vaccination or the traditional smallpox vaccine to stop the present monkeypox outbreak.

Disclosure of conflict of interest

None.

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