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Editorial

Chikungunya Fever: The Roles of Integrative Medicine in the Post-vaccine Era

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Chikungunya fever is becoming a major healthcare threat in more than 110 countries and may impact a total population of 2.8 billion, particularly those in East and Central Africa, South America, and Southeast Asia.[1,2] VLA1553 (live-attenuated, single-dose, trade name IXCHIQ) and PXVX0317 (purified virus-like particles, trade name Vimkunya) are the two approved vaccines for Chikungunya virus (CHIKV).[3–6] Their seroconversion rates were more than 95%, while their approval, accessibility, and indications differ across countries/regions.[5,6] They thus will shift the paradigm of CHIKV prevention and treatment.

Advances in the etiology, pathogenesis, and management of CHIKV were recently reviewed with a focus on traditional Chinese medicine in *Future Integrative Medicine* and *Journal of Integrative Medicine*, including these vaccines.[3,4] While touched upon by the reviews, the future roles of integrative medicine in the prevention and treatment of CHIKV are still worth reiterating in the post-vaccine era. This editorial thus focuses on these potential roles and may shed light on how to realize them in the future. It is also noteworthy that integrative medicine includes nutrition, rehabilitation, acupuncture, lifestyle care, symptom management, and other supportive approaches, as well as traditional Chinese medicine.

First, it will be very interesting and important to examine whether integrative medicine can help prevent and/or treat adverse effects of CHIKV vaccines. Both vaccines are overall safe. The trial shows that 1.5% of the participants receiving VLA1553 reported serious adverse events.[5] About 23–31% of the participants receiving PXVX0317 showed pain at the site of vaccination, with a higher incidence in adjuvanted vaccines.[6] However, recently reported severe adverse effects, including two deaths, raised concerns over their safety and even led to a safety review of VLA1553 in the UK.[7] The use of integrative medicine before or concurrently with vaccination may help prevent these adverse effects, but requires rigorous studies before clinical application.

Second, integrative medicine will continue to be an affordable and feasible approach to prevent and treat CHIKV infection in low- and middle-income countries. It is critical to increase vaccination rates among people at risk in the post-vaccine era, but there are several barriers. Regulatory reviews take time, resources, and effort. While necessary, they may delay vaccination in certain countries. Vaccine costs may also be prohibitively high, particularly in low- and middle-income countries, while chikungunya fever is more prevalent and vaccines are most needed in these countries. Before a low-cost CHIKV vaccine becomes available, integrative medicine should be rigorously studied and may be advocated in these countries. Indeed, the updates of China's guidelines on dengue and chikungunya diagnosis and treatment included integrative medicine and will further help advance and standardize its use.[8]

Finally, artificial intelligence (AI) should be more broadly and innovatively used to expand the roles of integrative medicine for chikungunya fever. The key barriers include the generation and curation of high-quality data, the use of external validation, concerns over bias and patient privacy, and the lack of AI experts in the field.

AI may help discover novel herbal medicines and compounds for preventing and treating CHIKV infection as more omics and chemical data become available. Advances in chemical analyses of herbal medicine and compounds will build a solid foundation for AI-assisted drug discovery. For example, African propolis was recently profiled using reverse-phase high-performance liquid chromatography and mass spectrometry.[9] Its chemical characteristics can then be used to identify potential molecular targets of African propolis. On the other hand, AI tools can help better understand and utilize the precise effects of herbal medicines and compounds on CHIKV at the omics level, as in herbal pharmacovigilance.[10]

AI can also help identify and manage patients with specific clinical outcomes in the post-vaccine era. It should become an important part of integrated care for CHIKV infection and disease. Three patient populations are particularly important. The first population will be the patients who would best respond to before-vaccination (versus concurrent) use of integrative medicine for reducing adverse effects of CHIKV vaccines. The second includes patients who would respond to integrative medicine, particularly during the subacute phase. The last population of interest includes patients at risk of chronic arthralgia or vaccine-related symptoms.

AI can help with many other aspects of preventing and managing CHIKV disease. It can facilitate better integration of integrative medicine into conventional/allopathic medicine for CHIKV, particularly using multimodal models. It may also reduce hesitancy

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toward integrative medicine according to patients' socioeconomic and religious characteristics in the post-vaccine era.

In the post-vaccine era, the prevention and treatment of CHIKV will be greatly changed. So will the roles of integrative medicine. Its research and use thus should be focused on adverse effects of CHIKV vaccines, while AI may further expand its roles. Integrative medicine can also be used as an affordable and feasible approach in the areas where vaccines are not approved, available, or widely accepted. However, integrative medicine should be studied as an adjunctive option, not as a replacement for vaccination, vector control (mosquitoes in this case), or evidence-based clinical care.

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Conflict of interest

The author declares no conflicts of interest.

Author contributions

LZ is the sole author of the manuscript.

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