Article Review

Advancements In Anti-Viral Strategies Against Nipah Virus

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ABSTRACT

Since its discovery in Malaysia during the epidemic of 1998, Nipah virus or NiV, member of paramyxoviridae family, has become one of the emerging potential threats to world health due to its uncontrolled rate of fatality and absence of specific therapies. The recent outbreaks in South and Southeast Asia have called for urgent international efforts to curb the virus. Since most infections with NiV bring about severe respiratory and neurological symptoms, treatment has relied on supportive care. There are no human vaccines available for distribution, though some preclinical trials and very limited human trial versions of vaccines are in development. This review article emphasizes on the recent advances in the therapeutic approaches and prevention measures of NiV. New treatment strategies like Defective Interfering Particles and RNA silencing, other than conventional treatments like antiviral drugs have also been discussed.

INTRODUCTION

The Nipah virus, an emerging zoonosis, has swept the world by storm as its very high rate of mortality and outbreak potential continues to amass increasing global attention. The virus was first identified in 1998 during an outbreak in Malaysia. It primarily affects animals like fruit bats, which are their natural reservoir, and pigs; however, the infections also occur in humans through direct contact with contaminated body fluids or infected animals (Pillai, Krishna, and Veettil 2020).

The outbreaks have been generally seasonal in Bangladesh, occurring usually between December and April, with a recent major outbreak at the start of 2024 from two cases, which proved fatal and are not otherwise related. In both cases, the history of consuming raw date palm sap had a known transmission vector because of contamination from fruit bats, the natural reservoir of the virus. There have already been such human-to-human transmission cases, especially in health care facilities, and the possible implications of even larger outbreaks are there, especially in highly densely populated areas of South and Southeast Asia.

The disease burden is futher complicated by the fact that there are no approved, effective treatments; once infected, the probability of survival is low, and survivors may have long term neurological issues that affect their quality of life and healthcare systems. The capability for higher outbreaks is maximized by its airborne transmissibility through respiratory secretions and human-to-human contacts, which may spark outbreak if an infected person travels (Talukdar et al. 2023). In fact, case fatality rates have been as high as 75%, hence posing a threat to public health on the international level, particularly in countries whose resources could not perform rapid detection and intervention (Alam 2022). It appears that there is bias in the fact that outbreaks of NiV occur more in the areas of fragile heath infrastructure thus increasing more difficulties in containment, treatments and prevention efforts.

Proactive Nipah virus research is critical for reducing mortality rates, containing outbreaks and preventing future pandemics. This type of research can equip the global community with the knowledge and tools necessary for rapid response, ultimately strengthening global public health resilience and protecting against the net potential zoonotic threat.

RESEARCH METHODS

Search in the online databases such as PubMed and GoogleScholar was performed to find related studies. Keywords used are as follows: Nipah virus, Nipah virus treatments, Nipah virus antiviral therapy, Nipah Immunotherapy, Nipah clinical management. Boolean operators were used to refine the search results. Peer-reviewed articles and case reports from the past five years (2019-2024) were reviewed.

RESULTS AND DISCUSSION

Current Approaches

Supportive Care: According to several sources, supportive care has remained the best approach so far for treating infection with Nipah virus (Urmi et al. 2023).

Antiviral Drugs: No specific antiviral drugs have been approved for Nipah virus, and development continues. Some in vitro and limited clinical experience have suggested that ribavirin is active; however, its effectiveness is still questionable (Pillai et al. 2020). Remdesivir, initially designed for Ebola, shows activity in animal studies (Johnson, Vu, and Freiberg 2021).

New Therapeutic Approaches

Monoclonal Antibodies: Monoclonal antibodies work by binding onto the virus with specific proteins that neutralize its entry into host cells. For Nipah virus, mAbs primarily target the viral envelope glycoproteins G and F, which serve as important sites for viral attachment and fusion to the host cells. Through glycoprotein blocking, mAbs prevent the entry of the virus into host cells and its subsequent replication.

Human monoclonal antibody m102.4 has shown much promise in models and now also tested in compassionate use protocols for treatment of patients (Johnson et al. 2021). Although m102.4 has been proven effective in animal models, but it requires larger human trails for further assurance of its safety and efficacy. There are also ongoing research being done to develop the next-generation mAbs, cheaper and more stable.

Defective Interfering Particles (DIPs): DIPs are mutants of viruses in which important parts of the virus's genome are missing, which makes it impossible for the DIPs to replicate themselves completely. Recent interest in DIPs is driven by their interference in the replication cycle of the original (wild-type) virus. Study showed DIPs reduced clinical signs and protected hamsters from lethal Nipah virus disease, thereby opening a new area for potential therapy (Welch et al. 2023). Research into DIPs for the treatment of Nipah virus has so far been very few; however, the general principle it suggests is that should DIPs be possible to engineer to compete better than NiV, this will inhibit its spread in the host.

Fusion Inhibitor Peptides: Fusion inhibitor peptides are mimetics of regions of the viral fusion glycoprotein in the process that triggers fusion, such as the heptad repeat regions called HR1 and HR2, in the fusion process. No fusion inhibitor peptides have yet been approved to treat NiV; however, they could be in clinical trials over the near future (Johnson et al. 2021).

RNAi: siRNAs are synthetic, double-stranded RNA molecules that are taken inside the host cell and, through incorporation into the RISC complex, bind the complex to the complementary sequence of the viral mRNA thereby leading to its degradation process that cannot translate into other necessary proteins in the virus. Through specific gene targeting for Nucleoprotein and L protein encoding genes found in the NiV genome, siRNAs efficiently diminish the viral replication in a cell. siRNAs targeting viral genes have also proven particularly promising in preclinical studies (Talukdar et al. 2023).

Preventive Measures And Vaccine Development

Public Health Measures: As put forth by scientists, the point of prevention does indeed fall on public awareness, surveillance, and hygiene education which eventually keeps the Nipah virus at bay (Welch et al. 2023).

One Health Approach: It aims at a multi-sectorial and inter-disciplinary understanding of the One Health strategy, which sees the relatedness between human, animal, and environmental health. There is natural transmission of nipah virus from fruit bats, which in turn give secondary infections to other animals or humans. One Health proposes monitoring the number of population of bats and studying pattern of viral shedding for estimating and reducing spillovers. Agriculturist practices are more directly involved in the transmission and are particularly risky in parts of the world where domestic animals and people live or are kept close together. One Health interventions can most effectively reduce risks of the transmission of contamination from infected food sources through implementing methods that protect sap and educating consuming communities on safe consumption techniques (Singhai et al. 2021).

Vaccine Development: Some vaccine candidates are currently in the preclinical stage, among them:

a. Mucosal Replicon-Particle Vaccine:

Mechanism: Stimulation of immune response in the mucous membranes where entry for the Nipah virus would be possible through self-replicating viral particles. Study demonstrated that a single dose of mucosal replicon-particle vaccine could safeguard against lethal infection of Nipah virus up to 3 days post-vaccination (Welch et al. 2023). The vaccine is still in preclinical studies of animals.

b. Live Attenuated Recombinant VSV Vector Vaccine:

Mechanism: Utilizes attenuated VSV as a vector to introduce Nipah virus proteins, which causes an immune response. Study established the immunological correlates of protection provided by PHV02, the live attenuated recombinant vesicular stomatitis virus vector vaccine for Nipah virus disease (Monath et al. 2023). The vaccine is in its preclinical research stage.

c. mRNA Vectored Vaccine:

Mechanism: Uses messenger RNA to instruct cells to produce Nipah virus proteins, triggering an immune response. Researchers have evaluated the immunogenicity of an mRNA vectored Nipah virus vaccine candidate in pigs, holding promising results. The vaccine is in preclinical stage (tested in pigs).

d. Fusion Protein Consensus Sequence Vaccine:

Mechanism: Targets the fusion (F) protein of Nipah virus using a consensus sequence approach to provide broad protection. Scientists developed vaccines based on the fusion protein consensus sequence. In preclinical studies, vaccinated Syrian hamsters were protected from Nipah virus infection (Lu et al. 2023).

e. Ferritin-Based Divalent Nanoparticle Vaccine:

Mechanism: Uses ferritin nanoparticles to present viral proteins in a highly organized manner, potentially enhancing immune response. During preclinical studies, scientists developed a highly potent ferritin-based divalent nanoparticle vaccine that was able to protect Syrian hamsters against lethal Nipah virus .

f. Recombinant VSV-Vectored Vaccine:

Mechanism: Similar to PHV02, uses VSV vector to deliver Nipah virus proteins. Preclinical research demonstrated that a recombinant VSV-vectored vaccine rapidly protects nonhuman primates against lethal Nipah virus disease (Foster et al. 2022).

g. Structure-Based Vaccine Design:

Mechanism: Uses structural biology approaches to design optimized paramyxovirus immunogens Researchers published a generalizable approach to the development of paramyxovirus immunogen through the structure-based design of Nipah virus vaccines in 2020 (Loomis et al. 2020).

h. Multi-Epitope Vaccine:

Mechanism: Combines multiple carefully selected viral protein fragments (epitopes) to generate broad immune responses. Scientists applied proteome-based strategy and defined candidates for the designing of a multitope vaccine against the Nipah virus in 2021 (Soltan et al. 2021). The vaccine is in theoretical phase based on proteome analysis.

Potential Therapies

Favipiravir Analogs: In silico studies on piperazine-substituted derivatives of favipiravir as potential inhibitors of the Nipah virus have been conducted by scientists in 2021 (Lipin et al. 2021). Phytochemicals from Herbs: Study screened herbal phytochemicals for developing a Rasayana for Nipah virus-induced immunity through traditional medicine for it (Debroy et al. 2023).

Cross-reactive humanized monoclonal antibody: Researchers generated a cross-reactive humanized monoclonal antibody, targeting the function of the fusion glycoprotein, which was shown to protect ferrets from lethal Nipah virus and Hendra virus infection (Mire et al. 2020).

Multi-targeted putative therapeutics: Scientists constructed NipahVR-a resource of multi-targeted putative therapeutics and epitopes for the Nipah virus that could potentially be used for the development of new treatments (Gupta et al. 2020).

CONCLUSION

Advances in the research area of the Nipah virus, from novel therapeutic approaches to vaccines, indicate promising findings, but with critical attention that requires urgent improvement. Monoclonal antibodies, especially m102.4, hold great promise in models involving animals. Novel approaches also include the use of Defective Interfering Particles and RNA silencing techniques, which provide further potential for therapies. The various platforms developed for a diverse vaccine such as replicon-particle mucosal approach, mRNA-based or nanoparticle approach-all critical steps made closer to the prevention of the virus spread, though all these fall under a preclinical study. Next priority should be on the expedited human clinical trials by promising candidates and designing more stable cost-effective formulations, stronger 'One Health' for a focus on prevention, and robust surveillance systems at all localities endemic. Success in the fight against Nipah virus will ultimately depend on sustained international cooperation, enhanced regional cooperation, improvement of healthcare infrastructure in vulnerable regions, and better integration of animal and human health surveillance systems. The above combination of strategies, along with stronger public health measures and research into novel therapeutic approaches, will be the best steps forward in reducing the burden of future Nipah virus outbreaks and protecting global public health.

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