Analysis Of Preventive Measures for West Nile Virus

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Abstract. The article explores the preventive measures for West Nile disease, starting with the origin of West Nile virus, first introducing the main processes of vaccine development, describing the two main types of vaccines: equine and human vaccines, citing research data showing the success of equine vaccine development, exposing the progress of human vaccine research, the possible problems, to whether there are studies confirming the breakthrough of this problem. The examples of two live attenuated vaccines are used to show the progress of vaccine development at this stage, and the problems and possible solutions to the vaccine are analyzed in light of its cost-effectiveness. Other preventive measures that are available to achieve the preventive effect are further analyzed, which are divided into two categories, the first being regional level protective measures by interfering with the transmission route, and the second being individual level protective measures by reducing contact with the source of transmission. The study data confirmed the need to maintain and strengthen bird monitoring programs, and ranked regional and personal precautions, analyzing the problems with regional precautions and the need for problem-specific ranking.

Keywords: West Nile Virus, Vaccine, Preventive Measures.

1. Introduction

West Nile virus is a flavivirus whose main vectors are mosquitoes and equids. According to information, West Nile virus was first isolated from a woman in the West Nile region of Uganda in 1937. Human infections caused by West Nile virus have been reported in many countries worldwide over the past 50 years. Approximately 80% of infected individuals are asymptomatic, but there is still the potential for subsequent exacerbation of the disease. Severe cases can develop into neuroinfectious disease with severe reactions such as high fever and coma, and adults over 60 years of age are more likely to develop neuroinvasive disease with high mortality or long-term neurological sequelae [1].

The West Nile virus disease is becoming more and more serious, which has aroused great concern of all countries. At the same time, the World Health Organization has listed it as one of the major global epidemics. At present, there is no method to treat human infection with the virus. New therapies based on tissue culture and animal models can only delay the progress of the disease to a certain extent and cannot be cured.

Vaccines are a preventive measure that allows the body to effectively acquire acquired immunity. Considerable progress has been made in the development of vaccines against West Nile virus. It is worth noting that West Nile is a flavivirus and developing a vaccine against it has similar problems as other flaviviruses: it is both space and resource intensive. Flaviviruses are complex biomolecular structures of more than one protein, nucleic acid, lipid, and carbohydrate molecule. This biomolecular structure means that producing a vaccine for it can be a more complex process [2]. In addition to the vaccine, the virus also has other preventive measures, such as cutting off the transmission route and reducing the final contact between the source of infection and human beings. This article will focus on the prevention measures of the virus, pay attention to prevention, actively strengthen publicity and education, and do a good job in personal protection.

2. Vaccine and clinical trial of West Nile virus

2.1. Equine vaccine

One of the main vectors of West Nile virus is horses, which means that West Nile virus is not only a threat to humans, but also to mammals, such as horses, which can cause serious symptoms. Therefore, a vaccine against West Nile virus should not only be given to humans, but also to animals like horses, which will not only provide effective protection to horses, but more importantly, will also play a role in interrupting transmission. Therefore, a vaccine against West Nile virus requires not only protection, but also strong immunity. There are at least four other types of WNV vaccines approved for use in horses since 2005, but no licensed WNV vaccines are currently available for use [2].

A study from Spain, on the other hand, focused on another host other than humans. The researchers collected 305 horses from three Andalusian provinces (Cadiz, Huelva and Seville), including 277 horses, 27 mules and 1 donkey. Through their investigation, the researchers found that 62 of these 305 samples had been previously vaccinated against West Nile virus, and by comparing IgG antibodies against flavivirus in the vaccinated and unvaccinated samples, they found significantly higher antibody levels and a significantly higher rate of individual seropositivity after vaccination than in the unvaccinated. This finding demonstrates that appropriate vaccination of horses is a remarkably effective preventive measure, and that the development of equine vaccines has been successful [3].

The success of equine vaccine development has provided valuable lessons for human vaccines, but the key problem to be solved for human vaccines is how to solve the problem of how to make the vaccine protective and cost effective while still having strong immunogenicity. The optimal solution to this problem is a vaccine that is only one dose in size and has a long duration of immunity. Therefore, how to select a vaccine with this or similar characteristics is a problem of research significance in this field.

2.2. Human vaccines

Only after a very rigorous review process is a vaccine allowed to join the national vaccine program. Each vaccine undergoes a review by the relevant authorities, and after the review, a score is assigned to determine the antigenic substances that trigger the appropriate immune response. Prior to the review, the relevant authorities will conduct tests on animals to evaluate and judge whether the vaccine is immune, and whether it is safe to use and has no potential side effects. If the vaccine passes the test and is proven to be effective, it will proceed to the next stage: human trials. There are three sections to this part [2].

Section one involves administering the vaccine to a group of young, healthy volunteers to determine that the vaccine has an immune effect and to control the vaccine at the correct dose. Section two will then increase the number of volunteers injected and assess the safety and immune effect of the vaccine by setting up a control group of volunteers of different ages. The third phase would be to administer the vaccine to larger and larger groups to examine the effect of the vaccine on the prevention of the virus of interest and its safety through comparison of larger numbers. After passing the appropriate clinical trials, approval and regulation by the health department and further studies by relevant department staff are required before the vaccine can be incorporated into the vaccine program [4].

One study described a variant of West Nile virus, "Isr98/NY99". This variant infects flocks of geese from three weeks to 10 weeks old and can cause massive paralysis and even death. The researchers initially vaccinated the geese with an attenuated flavivirus vaccine, which provided cross-protection but whose safety was questionable, so they produced a formalin-inactivated vaccine. Subsequent analysis found that the vaccine was effective in protecting the geese and that geese of all ages were able to survive the lethal conditions. The vaccine passed more extensive trials and was put into production [5].

Another study was a Phase II human trial data study of a live attenuated chimeric vaccine called ChimeriVax-WN02. Researchers divided a portion of the volunteers into four treatment groups and a portion into three different dose groups and continued to track data for up to six months after the vaccine was administered. Because the Phase I trial of the vaccine was selected in the age range of 18 to 40 years and proved to be well tolerated and highly immunogenic, the primary focus of the Phase II trial was on volunteers aged 50 years and older. The final study showed that the vaccine had neutralizing antibody titers with high seroconversion rates. Follow-up studies including vaccine efficacy measurements and larger sample sizes may be needed to confirm the true protective effect provided by the vaccine [6].

In summary for West Nile virus vaccine development, the trickier part is the phase III trial. The dynamics of West Nile virus transmission have shown that they are unpredictable in the short term, and although it is seasonal in nature, it still has two tricky issues: one is the short duration of the virus outbreak, which is extremely challenging for the establishment of a phase III trial. At the same time, there is uncertainty about the virus outbreak's location, which again adds to the Phase III trial's challenges [7].

One study was done with a live attenuated vaccine (rWN/DEN4Δ30). It is a chimeric virus that, after follow-up studies and comparisons, was found to have elevated levels of neurodegenerative properties. Twenty-eight volunteers aged 28 to 55 years were selected for the injection trial. Each volunteer received two doses of the vaccine and antibody performance was recorded from one month to one year after the injection. The final data showed that the vaccine was safe and strongly immunogenic, and the researchers concluded from their observations that a single dose of rWN/DEN4Δ30 produced prominent levels of neutralizing antibodies against WT WNV, which induced a 95% seroconversion rate in the elderly population. This has important implications for protection in the age group above 60 years [8].

2.3. Cost-effectiveness of the vaccines

After passing the appropriate clinical trials, the vaccine will need to be approved and regulated by the health department and further studied by the relevant department staff before it can be incorporated into the toxin trial. Once these issues are resolved, it is necessary to consider the cost behind the human trial. If this cost is maintained at an important level, the cost of the vaccine will be significantly increased, which means that people will have a significant financial burden to receive the vaccine. Once these issues are resolved, it is necessary to consider the cost behind the human trial. If this cost is maintained at an important level, the cost of the vaccine will be significantly increased, which means that people will have a significant financial burden to receive the vaccine. Thankfully, however, the data show that the live vaccines tested so far have an exceedingly high safety profile.

To address the cost-effectiveness of the vaccine, the researchers used Markov models to assess the cost performance of the vaccine for age and morbidity of the vaccinated person, as well as the potential cost per vaccine case prevented and QALY saved. The researchers divided vaccinators into two broad age categories: those over the age of sixty and others. They used age-specific West Nile virus neuroinvasive disease case data from 2004 to 2017 and calculated the percentages of disease acquisition and potentially preventable deaths for people older than 60 in each state and calculated annual composite incidence rates. The researchers analyzed and processed the data and found that the vaccine program was more cost-effective in states with a high viral burden than in the country as a whole or for specific populations [9].

3. Other prevention and intervention measures

In addition to vaccines, there are other preventive measures, which are divided into two main categories, one at the regional level and one at the individual level. These two categories are classified according to the path of transmission of the virus. Regional-level precautions are those that target the habitat of the source of infection and limit the spread of the virus from the source, in the path of transmission, such as measures in areas where mosquitoes gather; individual-level precautions are those that target the final contact between the source of infection and humans and reduce the spread of the virus by reducing personal contact with the source of infection.

The first step in source-specific protection measures is to determine what the primary source of transmission is. West Nile virus is transmitted during blood sampling from a vector that is the Culex mosquito and exists as a vector and an endemic cycle between certain birds as the primary amplifying host. Although both birds and humans serve as potential hosts, mosquitoes primarily feed on humans.

A study selected Thessaloniki as a regional area, investigated the mosquito species therein, and conducted tests. The researchers found 13 species of native mosquitoes belonging to four genera, with Culex pipiens being the most abundant, followed by Aedes caspius. The researchers examined the mosquitoes seasonally and found that the most abundant Culex pipens maintained a high population density throughout April to September. Aedes aegypti started to appear in early March and the highest numbers were seen from March to April, Culex pipens started to appear in April and lasted until July-August, and Anopheles pipens started to appear gradually and in high densities from August to October. According to the results, researchers believe that for an outbreak of West Nile virus in the region, the study of mosquito species and density will play a significant role in control and protection and can also help the study of the virus [10].

In addition to mosquitoes as the main source of infection, another point of concern is the birds. As a potential host for West Nile virus, some birds migrate periodically and some birds stay in their habitat, and these behaviors can have a positive effect on the virus. A study collected data on 1,842 dead birds from 2015 to 2019 in the Emilia-Romagna Region of Ferrara Province, Italy. These bird data were derived from a regional arbovirus surveillance program that included West Nile virus. The program uses fortnightly collection units to obtain information on mosquitoes through a network of fixed traps, monitor birds through active capture and passive collection of dead birds, and monitor cases of neurological diseases.

The researchers performed a viral test on all bird samples, collected data on the main organs of the birds and mechanically homogenized these samples, to collect real-time data, the researchers used PCR to monitor. The researchers collected data on species identification, date of collection, area where the sample was collected and date of death of the sample for each bird by category.

By sorting and counting the data, the researchers found that six species accounted for 91.4% of the total sample size, namely Passeriformes, Columbiformes, Falconiformes, Strigiformes, Apodiformes and Charadriiformes, with the most the most abundant were Passeriformes, and Falconiformes also occupied an outsize proportion. Further analysis of the data revealed that birds of the order Chickadees and Streptodactylus had the highest prevalence of WNV, with about 13%. In addition to the study of bird species, the researchers also counted the distribution of bird mortality and found that the highest number of birds tested positive for the virus was found between July and September, with the maximum number coming in the second week of August, a result that coincided with the peak mosquito season they obtained for the region. The researchers also found that passive detection of dead birds through, for example, cell phones is easier to implement and more cost-effective, while active detection requires a certain base of conditions to be implemented [11].

In the Spanish study, 171 wild birds were sampled, of which 56 (32.7% of the total) were found to have flavivirus IgG antibodies, and wild birds belonging to the eagle species had the highest frequency of seropositivity for West Nile virus (46% of the total), followed by Cicadelliformes, Strigiformes and Falconiformes, which, like the results of the previous Italian study, suggests that these birds are one of the more widespread species in Europe. In addition, the researchers found that species group, age and body size were the three main risks that could be related to West Nile virus exposure in wild birds, according to the model. Of these, raptor species were found to be 7.9 times more likely to be infected with the virus than other species because raptors are at the top of the food chain and have access to and feed on many potential hosts, meaning a greater risk of exposure, and the virus has been reported to cause mortality in threatened raptor species, such as the Iberian King

Eagle. Therefore, researchers recommend maintaining and enhancing surveillance programs for wild birds to better prevent future outbreaks of West Nile virus [12].

A Canadian study collected information on West Nile virus prevention and control in Quebec, Canada, and re-evaluated the interventions in the context of financial uncertainty and unclear virus trajectories, reassessing the actual situation and analyzing potential strengths and weaknesses. The researchers assembled a list of multiple targeted interventions, including proactive surveillance and targeted outreach, and summarized 15 evaluation criteria, each of which was assigned a range, to evaluate the listed interventions. The researchers divided the list of interventions into two categories and listed the top ones. The top-ranked measures for personal protection were regularly checking screen integrity, wearing light-colored clothing, spending less time outdoors during peak times, and cleaning up surrounding mosquito habitat in a timely manner. These measures scored high on most scales. Vaccine scores were exceptionally low, including concerns about cost, consequences of vaccination, and other aspects that caused unusually low scores on many scales. Another broad category is regional level interventions. The top three interventions were larvicides, animal host vaccination, and modification of artificial larval sites.

When the two categories were ranked together, the regional-level interventions were ranked low compared to the individual rankings, with most of the top overall rankings being for individuals. The researchers found that individual-level interventions did not show significant differences across scenarios. This stability suggests that the corresponding individual interventions are still effective and acceptable and should be sustained in dissemination activities, with the possible problem that they require a certain financial base but are acceptable to most households. Interventions at the regional level are stable, although subject to change, as the intensity of dissemination increases. But the potential costs required for these interventions such as measures such as retrofitting sewers can be very costly and may have certain negative effects of other situations. The researchers confirm that individual interventions are consistent across studies, but that regional-level measures need to be analyzed on a case-by-case basis in outbreak areas [13].

4. Conclusions

In conclusion, the main protection measures against West Nile virus are vaccines and interventions. The vaccine for humans is still in the development phase, and the main problem is in the third phase of human trials, with specific adjustments according to the actual situation in the respective outbreak areas. There is also a need to reduce the cost effect of the vaccine, individual treatment at this stage generates extremely inflated costs, and only when costs are controlled can such a human vaccine be truly put on the market and vaccine program.

Interventions are divided into two main types, a regional level intervention, in the source of infection and transmission routes, through the main source of transmission of mosquito species research, monitoring, to determine the seasonal factors of the outbreak, to the mosquitoes to intervene accordingly. By studying the species of potential host birds, the period of active mosquitoes is again determined by the peak of infection in birds, and this is used to find interventions for birds. Finally, there are individual interventions, through which the top-ranked interventions can be more effective and have a more stable performance at different intensities of infection.

References

[1] West Nile virus https://www.who.int/news-room/fact-sheets/detail/west-nile-virus.

[2] West Nile Virus Vaccines https://www.niaid.nih.gov/diseases-conditions/wnv-vaccines.

[3] García-Bocanegra I, Franco JJ, León CI, Barbero-Moyano J, García-Miña MV, Fernández-Molera V, Gómez MB, Cano-Terriza D, Gonzálvez M. High exposure of West Nile virus in equid and wild bird populations in Spain following the epidemic outbreak in 2020. Transbound Emerg Dis. 2022 Oct 12.

[4] H ow are vaccines developed? https://www.who.int/zh/news-room/feature-stories/detail/how-are-vaccines-developed.

[5] Samina I, Khinich Y, Simanov M, Malkinson M. An inactivated West Nile virus vaccine for domestic geese-efficacy study and a summary of 4 years of field application. Vaccine. 2005 Sep 30;23(41):4955-8.

[6] Dayan GH, Bevilacqua J, Coleman D, Buldo A, Risi G. Phase II, dose ranging study of the safety and immunogenicity of single dose West Nile vaccine in healthy adults ≥ 50 years of age. Vaccine. 2012 Oct 19;30(47):6656-64.

[7] Kaiser JA, Barrett ADT. Twenty Years of Progress Toward West Nile Virus Vaccine Development. Viruses. 2019 Sep 5;11(9):823.

[8] Pierce KK, Whitehead SS, Kirkpatrick BD, Grier PL, Jarvis A, Kenney H, Carmolli MP, Reynolds C, Tibery CM, Lovchik J, Janiak A, Luke CJ, Durbin AP, Pletnev AG. A Live Attenuated Chimeric West Nile Virus Vaccine, rWN/DEN4Δ30, Is Well Tolerated and Immunogenic in Flavivirus-Naive Older Adult Volunteers. J Infect Dis. 2017 Jan 1;215(1):52-55.

[9] Curren EJ, Shankar MB, Fischer M, Meltzer MI, Erin Staples J, Gould CV. Cost-Effectiveness and Impact of a Targeted Age- and Incidence-based West Nile Virus Vaccine Strategy. Clin Infect Dis. 2021 Nov 2;73(9):1565-1570.

[10] Spanoudis CG, Pappas CS, Savopoulou-Soultani M, Andreadis SS. Composition, seasonal abundance, and public health importance of mosquito species in the regional unit of Thessaloniki, Northern Greece. Parasitology Research. 2021;120(9):3083-3090.

[11] Lauriano A, Rossi A, Galletti G, Casadei G, Santi A, Rubini S, Carra E, Lelli D, Calzolari M, Tamba M. West Nile and Usutu Viruses' Surveillance in Birds of the Province of Ferrara, Italy, from 2015 to 2019. Viruses. 2021; 13(7):1367.

[12] García-Bocanegra I, Franco JJ, León CI, Barbero-Moyano J, García-Miña MV, Fernández-Molera V, Gómez MB, Cano-Terriza D, Gonzálvez M. High exposure of West Nile virus in equid and wild bird populations in Spain following the epidemic outbreak in 2020. Transbound Emerg Dis. 2022 Oct 12.

[13] Hongoh V, Campagna C, Panic M, Samuel O, Gosselin P, Waaub JP, Ravel A, Samoura K, Michel P. Assessing Interventions to Manage West Nile Virus Using Multi-Criteria Decision Analysis with Risk Scenarios. PLoS One. 2016 Aug 5;11(8):e0160651.