Proposal for the control and prevention of Eastern Equine Encephalitis for equines and humans in Ecuador.

Propuesta de control y prevención de Encefalitis Equina del Este para equinos y humanos del Ecuador

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Abstract: The objective of this research was: To make a proposal for the control and prevention of Eastern Equine Encephalitis (EEE) for equines and humans in Ecuador, a search was applied in four electronic databases in search of publications on the proposed topic that met the inclusion criteria for the systematic review. Subsets of publications were subjected to a meta-analysis to determine the best information on the topic. A total of 172 references published between 1938 and 2021 were included. EEE was reported throughout the Americas, from Canada to Argentina with publications on natural infections since 1933, where it was first isolated in the U.S., is now endemic in North America, and reaches South American ecosystems via infected migratory birds. EEE is a notifiable disease, and causes fatal meningoencephalitis in equines and humans; therefore, successful control of this arbovirosis is important.

Keywords: VEEE, EEE. control and prevention, epidemiology, epidemiology.

Resumen: La presente investigación tuvo como objetivo: Realizar una propuesta de control y prevención de Encefalitis Equina del Este (EEE) para equinos y humanos del Ecuador, se aplicó una búsqueda en cuatro bases de datos electrónicas en busca de publicaciones sobre la temática propuestas que cumplieran con los criterios de inclusión para la revisión sistemática. Se sometieron subconjuntos de publicaciones a un metaanálisis para determinar la mejor información sobre el tema. Se incluyeron un total de 172 referencias publicadas entre 1938 y 2021. Se notificó EEE en todo el continente americano, desde Canadá hasta Argentina con publicaciones sobre infecciones naturales desde 1933, donde se aisló por primera vez en los EEUU., ahora es endémica en Norteamérica, y llega a ecosistemas sudamericanos a través de las aves migratorias infectadas. La EEE es una enfermedad de declaración obligatoria, y causa meningoencefalitis fatal en equinos y humanos; por lo consiguiente, es importante un control exitoso de esta arbovirosis.

Palabras clave: Marketing, production, cocoa, export, positioning.

Introduction

The Eastern Equine Encephalitis Virus (*EEEV*) causes Eastern Equine Encephalitis (EEE) which is characterized by causing febrile disease accompanied by fatal encephalitis in equines and humans, with mortality percentages that can reach in humans between 30 to 70% (OIE, 2017, p. 16) and in equines between 70 to 90% (CFSPH, 2010, p.11Bingham et al., 2014; CFSPH, 2017, p. 12), therefore, it is considered the most deadly arbovirus (virus transmitted by arthropod vectors), in addition, it has an incubation period between 5 to 14 days (OIE, 2017, p. 16).

The *VEEE* belonging to the *Togaviridae* family, *Alphavirus* species, generally has an enzootic cycle and usually appears in Latin American ecosystems when infected migratory birds (amplifying hosts) arrive to the wetlands and transmit the virus to native birds, preferably through mosquitoes of the genus *Culex*, however, the infected vector bites domestic and wild animals, being the susceptible hosts to the disease, equines and humans (PAHO/WHO, 2017).

Transmission of *EEEV* involves several birds of the order *Passeriformes* and *Columbiformes* (Molaei et al., 2013), 26 species of mosquitoes, lice and chicken mites (CFSPH, 2017, p. 12), amphibians, reptiles (Bingham et al., 2014) and mammals such as wild rodents, marsupials, opossums (Mesa et al., 2005), bats (Blohm et al., 2018; Benvenuto et al., 2019), monkeys, dogs, goats and small mammals; also, occasional cases of encephalitis have been reported in sheep, cattle, deer, South American camelids (llamas and alpacas) and pigs. (Go et al., 2014). Thus, *EEEV* can establish a transmission network between several bird species, several reservoirs, several vectors and susceptible hosts (Coello et al., 2020).

The virus was isolated for the first time, in 1933 in horses in New Jersey in the United States (USA) (Feemster, 1938, p. 8; Fulton, 1940, p. 7), in 1955 in this country it was isolated in mosquitoes, rodents and humans and in 1960 in birds according to Casals (1964, p. 19) and Armstrong and Andreadis (2013, p. 4), then in 1982 it was isolated in dogs (Weaver et al., 1994).

EEE in humans presents with fever, headache, irritability, stiff neck, confusion, drowsiness or stupor, focal neurological impairment, disorientation, tremors, convulsions and paralysis, although some patients go into coma, also, palpebral edema, abdominal pain, vomiting and diarrhea may be observed (CFSPH, 2010, p. 11). In animals the disease presents with: High fever, malaise, malaise, dullness, depression, lack of appetite, aimless walking, often in circles, head pressure at corners, blindness, staggered and uncoordinated gait, reclining, convulsions and death (in over 80% of cases) (Mackay, 2017, p. 91).

The Eastern Equine Encephalitis Virus is prevalent in the Americas from Canada to Argentina, distinguishing 5 viral subtypes with high virulence and genetic variability (Mesa et al., 2005). Between January 1 and October 20, 2020, the CDC reported 9 confirmed cases of EEE in the USA, with cases in Indiana (1), Massachusetts (4), Michigan (2) and Wisconsin (2). (CDC, 2021). The purpose of the present work is to carry out a Proposal for the control and prevention of Eastern Equine Encephalitis for equines and humans of Ecuador .

Materials and methods

The systematic review (SR) and meta-analysis (MA) were conducted according to inclusion and exclusion criteria that were defined based on the relevance of the references to achieve the study objectives. A systematic search was performed to identify all publications reporting on EEE and Proposals for equine and human control and prevention. Four electronic databases were searched: CAB Abstracts , Library of Institute of Tropical Medicine (EDS-ITM) , PubMed and ScienceDirect using the search terms "EEEV or EEE and Control and prevention" applied for all article content. No restrictions were applied with respect to language, location, and date of publication (the last search was performed on April 21, 2021). In addition, additional manual searches of author collections of relevant peer-reviewed publications were included. Duplicate references with the same information about what was found in the corresponding searches were eliminated, and abstracts were also obtained for certain references.

Result

Among the proposals for the control and prevention of Eastern Equine Encephalitis for equines and humans in the country, we have:

Awareness of the disease in rural and wild areas: Explain the disease and its impact on the environment through talks to the inhabitants of sectors at epidemiological risk (Coello et al., 2020).

Measures to prevent the spread of EoE: The most important control measure is to reduce the source of infection by biting the vector; therefore, insecticidal compounds (such as Detan) and heavy clothing should be used to prevent transmission (CDC, 2021).

To make it known that migratory birds are amplifiers of EEEV: Migratory birds are the animals that amplify the virus and carry the infection to places where there were no cases before. It is necessary that migratory birds should be free and allowed to continue their passage through the sector, without the need for them to be captured or killed for sporting or hunting purposes (Reisen et al., 2010).

To teach about the hosts susceptible to EEEV and what are the warning signs in case of suspected cases of EEE in the sector: Susceptible animals are birds, dogs, horses and humans, in the latter two it produces encephalitis (Go et al., 2014). On the other hand, birds (Williams et al., 1971) and equines (Monath et al., 1985) are considered sentinels of the disease (the first cases always appear in them); therefore, they are indicators of suspected cases of wild arbovirosis, and preferably, they occur in sectors with an immense ecological biodiversity where migratory birds arrive (Santander, 2009, p. 11; Coello et al., 2020).

To make known, which are the most common hosts to investigate VEEE in the field: they are Migratory birds, native birds, mosquitoes, rodents, domestic dogs, equines and humans (OIE, 2017, p. 16; Benvenuto et al., 2019).

To find out if there is viral circulation in the area: This is done through investigations or inquiries about deaths and clinical characteristics of sentinel animals in the sector; also, hamsters and chickens can be placed as sentinels, with the purpose of infecting them, in order to then take samples from them and

subsequently attempt viral isolation in cell cultures and animals in the laboratory (OIE, 2017, p. 16).

To find out if any host is infected or has been infected by VEEE: Samples should be taken from sentinel animals and antibodies for VEEE should be determined or viral detection should be performed. To identify antibodies, the ELISA test is performed and for viral detection, the PCR technique is used. (Benvenuto et al., 2019) .

Capture of migratory and domestic birds: Migratory and sector birds are caught with CDC-type mist nets and domestic birds by hand pulse (OIE, 2017, p. 16).

Carry out mosquito trapping: It is performed with CDC type mosquito traps, supplemented with CO2, placed from 6 pm to 6 am (Hoyos et al., 2015).

Placement of sentinel animals for field research: In field research for arboviruses, cages with animals (chickens or hamsters) are also placed generally at a height between 1 to 2 meters attached to trees and near the estuary, so that infected mosquitoes infect the animals through bites (Hoyos et al., 2015; OIE, 2017, p. 16).

Rodent trapping: This is done with Tomehawk traps for larger animals such as opossums, and Sherman traps for small animals (rodents) (Arrigo et al., 2010).

Procedure for taking samples from animals and humans: For domestic animals, permission must first be requested from the owners of the animals; in the case of wild animals, permission must be requested from the Foundation that protects the animals and the Ministry of the Environment. In the case of humans, permission must also be requested. Prior consent, for equines the blood sample is taken from the jugular vein, for dogs from the jugular, saphenous or popliteal vein, and for birds from the jugular or wing vein. In humans, the blood sample is taken from the median vein, following procedures described by the OIE, PAHO/ WHO and CDC.

Blood samples are conducive for serological studies and viral detection, but in cases of equine and human encephalitis the best sample is Cerebrospinal Fluid or brain tissue (OIE, 2017, p. 16).

Attempted viral isolation: From a brain sample of the deceased equine by encephalitis, viral isolation can be done in cell culture (BHK-21, Vero, C636 cells) where cytopathic effects are evidenced; or intraparietal viral inoculation in 48-hour-old suckling mice, where after 3 days we observed signs and symptoms of disease (OIE, 2017, p. 16; Benvenuto et al., 2019).

Diagnosis for VEEE in various hosts: Laboratory diagnosis is effective to determine the disease in the area and to differentiate from other arboviruses. Therefore, two methods should be followed: Indirect method (antibody detection) and direct method (viral detection) (OIE, 2017, p. 16).

Indirect methods include: ELISA, Indirect Hemagglutination, Indirect Immunofluorescence, and the confirmation of antibodies is performed by the method of Neutralization by Reduction of the Number of Plates. It is important to mention that all arboviruses need to be confirmed due to the intense cross-reactivity among them, because the epitopes (antigens) are very similar (OIE, 2017, p. 16; Benvenuto et al., 2019).

Direct methods include: Viral Culture, Electron Microscopy, Direct Hemagglutination, Direct Immunofluorescence and PCR (OIE, 2017, p. 16).

Training of health professionals is important in order to be prepared for suspected cases of arbovirus (PAHO/WHO, 2017).

Periodic investigation in sites of epidemiological impact: It is recommended to investigate direct and indirect viral activity in sentinel animals at least, every year coinciding with the arrival of migratory birds in the sector (OIE, 2017 p. 16; PAHO/WHO, 2017).

How to acquire immunity for EEE in equines: In equines it is by vaccination. In contrast, in humans there is no vaccine for the disease (OIE, 2017, p. 16).

Where to go in case of suspicious outbreaks: In case of suspicious cases, it is recommended to inform the epidemiological surveillance systems of Agrocalidad, the Ministry of Public Health of Ecuador and the Ministry of Environment (OIE, 2017; PAHO/WHO, 2017).

The control and prevention proposal exposed, about Eastern Equine Encephalitis for equines and humans, is with the purpose of raising awareness about a possible introduction of this disease in Ecuador and in the American continent; in this way, the present study allows to contribute with knowledge about control and prevention of EEE and to avoid future outbreaks. Therefore, when a suspicious case is registered, we can be alert to any warning signs of the disease, in order to take all appropriate and effective measures to deal with the disease, as is done in North American countries (Bingham et al., 2014; Gill et al., 2019; Morens et al., 2019).

The points suggested in this article are taken according to OIE (2017, p. 16) / PAHO and WHO (2017) / and CDC (2020) criteria.

It is also important that the community is prepared for these cases, and inform the epidemiological surveillance systems of the EEE in Agrocalidad, Ministry of Public Health of Ecuador and Ministry of Environment.

Finally, it is transcendental to highlight that in the human and equine population there is a risk of Eastern Equine Encephalitis, although it is currently in epidemiological silence and could cause epizootics or re-emerging epidemics in a very short period of time.

Conclusions

A proposal was made for the control and prevention of Eastern Equine Encephalitis for equines and humans in Ecuador, which can be used by the scientific community and especially for communities living in wild places.

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