OPEN ACCESS Journal of Animal Health and Production

Review Article

A Review of Rabies Disease, its Transmission and Treatment

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Abstract | The rabies is an infectious disease, which defects brain caused by the virus known as lyssavirus belonging to family *Rhabdoviridae*. It is a semi zoonotic acute disease because the rabid animal dies after illness. It is transmitted by all homoeothermic animals and virus is secreted in the saliva of an infected animal. However, dogs are considered as high risk while in America, bat bites are also the cause of spread of rabies. The incubation period of this disease is approximately up to six months long or in some cases, it is short up to just four days. Symptoms are produced after completion of the incubation period. The virus gets entrance in the brain and causes damage there, after that it moves toward salivary gland in order to transmit in other animals while biting or due to contamination of saliva of an infected animal. The clinical signs and symptoms of this disease could be confused with some other diseases such as polio, tetanus, and botulism. Hence, confirmatory diagnosis is done by using techniques including polymerase chain reaction, direct fluorescent antibody test, and mouse inoculation technique. This paper reviews the transmission, pathogenesis, control, prevention and treatment of rabies since it is a highly fatal disease so preventive measures could be taken to fight against this infection.

Keywords | Rabies, Transmission, Treatment, Control, Review

Editor | Asghar Ali Kamboh, Sindh Agriculture University, Tandojam, Pakistan.
Received | September 15, 2016; **Accepted** | October 02, 2016; **Published** | October 27, 2016
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Citation | Bano I, Sajjad H, Shah AM, Leghari A, Mirbahar KH, Shams S, Soomro M (2017). A review of rabies disease, its transmission and treatment. J. Anim. Health Prod. 4(4): 140-144.
DOI | http://dx.doi.org/10.14737/journal.jahp/2016/4.4.140.144
ISSN | 2308–2801

The rabies is a well-known viral infection which is affecting the central nervous system of all animals which are warm-blooded in addition to humans (Moges, 2015; Richard et al., 2015). The rabies is a zoonotic disease which leads to fatal encephalitis in mammals (Chernet and Nejash, 2016). The infection is characterized via the appearance of rigorous nervous symptoms that results in paralysis following the death of the patient (Abera et al., 2015). Once symptoms of the virus extend, it is always lethal disease which can be only prevented but unfortunately incurable (Chernet and Nejash, 2016). The canines especially dogs remain the primary reservoir in rising countries, while, wildlife species act as hosts in developed nations (Rupprecht et al., 2007).

ETIOLOGY

The causative agent of rabies is *Lyssavirus* genus belonging to the *Rhabdoviridae* family. It is a bullet shaped virus, containing a single-stranded RNA genome (Nilsson, 2014; Moges, 2015). The lyssavirus is prone to the ultraviolet radiation. It is speedily inactivated by exposure to air, sunlight and in dried blood with secretions (Tojinbara et al., 2016).

EPIDEMIOLOGY

According to a number of investigations, about 55,000 people die due to rabies in Africa and Asia each year.

The collective immunization of pet dogs along with cats at predictable expenses of approximately 300 million dollars in huge division accounts in favour of the lower rate of rabies in human inside the United States (Coleman et al., 2004). Furthermore, the wild animals including bats, raccoons, foxes and skunks accounted more than 92% of rabies caused by animals in cases presented to the United States Centers for Disease Control and Prevention (CDC) in 2005 (Blanton et al., 2008). Rabies due to terrestrial animals in the United States is most widespread in raccoons resting on the eastern coast and within foxes, skunks, coyotes, in addition to dogs on the Texas-Mexico border. The canine rabies, as well as bat rabies, are momentous problems within Mexico and around the world (Smith, 1996). The rodents in the United States that can clutch rabies virus long enough in the direction of human transmission, other small rodents (*e.g.* squirrels, chipmunks, rats, mice) and lagomorphs (*e.g.* rabbits, hares) usually die before being able to transmit rabies virus to humans, and human disease has not been documented from these mammals (Blanton et al., 2007).

MODE OF TRANSMISSION

The lyassa virus infection is transmitted by all animals who are considered as warm-blooded, while the lyssavirus can also grow up in cells of cold-blooded animals (Mustafa et al., 2015). The transmission of this disease requires entrance of virus through the saliva of an infected animal due to biting, wounds or unwrap cuts in fur or mucous membranes (Langley, 2009). Rabies disease is not a true zoonotic disease as the infected animal dies due to severe infection (Sikes, 1962). An investigation of infected dogs within the USA revealed that the all rabid dogs died within just 8 days of becoming infected. Nearly the entire transmissions are by means of bites. Since the virus is secreted in saliva, the disease can rarely arise through scrape contaminated by saliva; while the disease rate is 50 times lower (Eng and Fishbein, 1990; Fishbein, et al., 1993). The spread of the virus from individual to individual is very rare, however, a small number of cases were recorded as a result of transplant surgery (Srinivasan et al., 2005).

PATHOGENESIS

The lyssavirus enters the body via abrasions or by direct in touch with mucosal membranes. It is not able to intersect undamaged skin. The rabies virus replicates inside the bitten muscle tissue and then it achieves entry towards the central nervous system (Ugolini, 2007). The virions are passed in carrying vesicles (Klingen et al., 2008) and move to the central nervous system (CNS) completely via rapid retrograde transport beside motor axons, by means of no uptake through sensory or sympathetic endings (Hemachudha et al., 2013). The entrance of virus inside tissues of the brain leads to death, usually through respiratory dysfunction and secondary metabolic and circulatory defects (Bishop et al., 2003; Shite et al., 2015).

CLINICAL SIGNS

It is investigated that as the disease becomes advanced, the animal shows strange behaviour. Every verified suspicion of rabies must be established by the confirmatory report of laboratory test (Chernet and Nejash, 2016). The primary clinical signs are frequently non-specific and can comprise anxiety, restiveness, anorexia or an improved appetite, nausea, diarrhea, a minor fever, dilation of the pupils, hyperactivity to any stimuli in addition to extreme salivation. The initial sign of post-vaccinal rabies is generally lameness in the vaccinated limb. The animals regularly comprise behaviourally and personality changes, and might turn into either curiously aggressive or uncharacteristically dedicated (Banyard et al., 2013).

Prodromal Stage

Following a definite incubation phase, the beginning of clinical symptoms starts. During this first stage which typically ends within 1-3 days, slight behavioural modification may occur, *i.e.* anger in domestic animals, daytime tricks in nocturnal animals, no fright of humans in the wild animals or else irregularities in the appetite (WHO, 2013).

Excitement (Furious) Phase

The furious type is described via agitation, wandering, weeping, polypnea, drooling and attacks upon other animals, community or unresponsive objects. Infected animals frequently ingest foreign items for instance firewood and gravels. The wild animals often drop their fright of humans, and may harass humans or another surrounding animal that they would usually avoid (*e.g.*, porcupines). On the other hand, the nocturnal animals may be observable throughout the day. In cattle, strange attentiveness can be an indication of this phase (Banyard et al., 2013).

Paralytic (Dumb) Phase

The "dumb" type of rabies is usually characterized by the progressive paralysis. In this phase, the gullet and masseter muscles turn into paralyzed; the animal might be incapable of swallowing, and salivating abundantly. There may be a change in voice of infected animal due to laryngeal paralysis, including atypical bellowing in cattle and barking in dogs. In addition to that, there might be facial paralysis along with dropping of the lower jaw. Ruminants may become isolated from the herd (Yang et al., 2012). Furthermore, this stage is also characterized by dropping of foamy salivary secretion and paralysis of hind limbs eventually leading complete paralysis followed by death (WHO, 2013).

Hydrophobia

The term stands for the fright of water is the historic synonym of rabies (Smallman-Raynor et al., 2004). This condition refers to a collection of warning signs during the advanced phases of an infection in which the patients have obscurity in swallowing and taking water. Any mammal infected by the virus may reveal hydrophobia. In this condition, there is over production of saliva, and animal struggles to drink and could suffer from painful spasms of the muscular tissues within the throat as well as in vocal cord. The virus remains in saliva and is spread due to bite of rabid animal (Mustafa et al., 2015).

DIAGNOSIS

This disease can only be identified following the onset of the symptoms (WHO, 2013). The diagnosis of rabies is carried out by either *in vivo* or through autopsy (Consales and Bolzan, 2007). The lyssavirus infection is not easy to diagnose via ante-mortem. While the hydrophobia is extremely suggestive, furthermore no medical signs of infection are pathognomonic for this disease. The historical reliance resting on the finding of accumulated Negri-bodies is no longer considered as appropriate in support of the diagnostic evaluation, since of short sensitivity and alternative some laboratory- based test have been developed for confirmation of infection (Abera et al., 2015). The diagnosis of rabies virus is made by taking some part of tissue from the brain of suspected animal. But mostly for confirmatory diagnosis samples from the brain stem and cerebellum are taken (Yousaf et al., 2012). The brain smears are utilized for the human discovery of virus antigen by means of the fluorescent antibody test (FAT), designed mutually for human as well as for animal samples. In most animals, the direct FAT is suggested as a confirmatory diagnostic test. Other methods for detection of this virus are mentioned in Table 1.

PREVENTION AND CONTROL

The vaccine against rabies was invented in 1885 by Louis Pasteur along with Emile Roux, prior to which nearly all human cases of rabies were lethal. The creative vaccine was produced by infected rabbits. In this procedure, the virus in the nervous tissue of rabbits was damaged by permitting it to dehydrate for about approximately five to ten days (Geison, 1978). Furthermore, the human diploid cell rabies vaccine was discovered in 1967. While nowadays chicken embryo cell vaccines are available which are cheap (Ly et al., 2009). Another recombinant vaccine known as Raboral V-RG is in use within France, Belgium, Germany, in addition to the United States to avoid outbreaks in wild animals (Reece et al., 2006). Human rabies can be stopped by supplying suitable rabies pre-exposure prophylaxis, and timely local treatment of infected lesions combined in the company of proper rabies post-revelation prophylaxis (Tojinbara et al., 2016). The non-activated man vaccines are presented for veterinary workers, animal trainers, wildlife representatives, laboratory employees and others which are at higher risk of exposure (Chernet and Nejash, 2016).

PROGNOSIS

In non-vaccinated humans, rabies is constantly deadly following neurological warning signs developed. The vaccination following experience, post-exposure prophylaxis (PEP), is extremely victorious for prevention of the disease if introduced within 6 days of illness. In the case of the major hindrance in control of PEP, the treatment still has a possibility of victory (Mustafa et al., 2015).

TREATMENT

Just the once rabies warning signs have appeared, the treatment is generally supportive. The patients are sedated to manage their fear and pain. The basis of treatment is serious care support, counting paralysis, sedation, as well as ventilation. The ketamine is mostly suggested as a suitable mediator for these conditions (Jackson et al., 2003). Lyssavirus is simply inactivated by the sunshine, soap, in addition to aeration. The wound concern is essential for the hindrance of rabies infectivity. Among the investigational animals, rabies spread could nearly wholly have prohibited via general wound treatment provided during the first 3 hours following disclosure of virus (Dean et al., 1963). The injured area should be rinsed carefully with antiseptic soap and water. After that povidone-iodine or alcohol should be applied in order to reduce the virus further (Gautret et al., 2014).

Table 1: The diagnostic techniques for rabies disease

Techniques	Sample	Benefits/ disadvantages
Polymerase Chain Reaction (PCR)	body fluids, saliva, urine, cerebrospinal fluid	Applicable in all tissue conditions but, requires experienced technicians
Mouse Inoculation Technique (MIT)	liver, brain, salivary glands, spleen and pancreas are the most appropriate sample	In this technique only fresh tissue is used for an accurate result
Direct Fluorescent Antibody Technique (DFA)	Similar to MIT	Applicable with most tissue sources. Not applicable in decomposed tissues.

Source: Yousaf et al. (2012)

The CDC suggested a dose of human being rabies immunoglobulin (HRIG) which should be introduced in the region of the bites, by means of deep intramuscular booster on spot other than the vaccination spot (Mustafa et al., 2015).

CONCLUSION

The rabies is a viral disease which is fatal in nature, among unvaccinated human as well in animals. It can be controlled by proper awareness and immunization against the lyssavirus in both farm animals as well as pets. Rabies can be prevented by avoiding direct contact with the rabid animal, its mucous membranes, and wounds and by giving proper training to wildlife workers, veterinarians, animal handlers and laboratory workers because prevention is better than cure.

ACKNOWLEDGMENTS

I want to thank my all co-authors for their help and contribution.

CONFLICT OF INTEREST

There is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors were very co-operative and we collected information related to this review paper collectively.

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