

PPRV: Sign and Symptoms, Prevalence and Possible Treatment with Different Plants

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ABSTRACT

The disease Peste des petitsruminants (PPR) is an extremely spreadable and it is liable for high illness and even causes death in sheep and goats. The disease is caused by Peste des petitsruminants virus (PPRV). This virus can be spread from infected animals to the vulnerable animals by exhaled aerosol or clinical excretions. Signs and symptoms of PPR included pyrexia, stomatitis, diarrhea, ulcerative lesions and oculo nasal discharge. In the current paper we reviewed the prevalence of virus in all over world especially Pakistan along with its treatment by utilization of different plants.

Keywords: PPRV, prevalence, possible treatment, plants

INTRODUCTION

Peste des petits ruminants (PPR) is also recognized as 'goat plague', 'Kata', 'syndrome stomatitis-pneumoenteritis' of or 'ovine rinderpest' (Parida S. et al, 2015). The disease Peste des petitsruminants (PPR) is an extremely spreadable and it is liable for high illness and even causes death in sheep and goats. The family of PPRV is Paramyxoviridae with genus Morbillivirus. Measles virus, rinderpest virus, canine distemper virus, phocine distemper virus and dolphine and porpoise morbilliviruses are all related to Morbilliviruses. Virus neutralization test (VNT) is a test recommended for the recognition of PPRV antibody; it is tedious and costly and needs infectious virus. So VNT is not ideally suggested as a daily procedure. Many competitive enzyme-linked immunosorbent assays (c-ELISAs) have been known as appropriate diagnostic tool and utilized for sero epidemiological surveillance as they are easy, highly sensitive as well as economical (Abubakar et al, 2009).

Some other diseases including rinderpest, bluetongue and contagious caprinepleuro pneumonia, can be misunderstood with Peste des petits ruminants due to the resemblance of clinical sign and symptoms of these diseases. There is a chance of secondary bacterial infections that makes the diagnosis of the disease complicated, so laboratory diagnostic techniques used in addition with clinical observations to confirmed diagnosis. There are three categories in which laboratory test that are currently available can be grouped for diagnosis: (i)test based on the detection of virus or viral antigen (ii) test based on the detection of genetic material from the virus and (iii) test based on the detection of antibodies against the virus (Parida S. et al, 2015).

PPRV antibodies can be detected by ELISA techniques. Beside ELISA some other techniques also present including latex agglutination test, haemagglutination test, novel sandwich ELISA and immunofiltration. PPRV antigens can be detected by counter immune electrophoresis (CIEP), immunecapture ELISA (ICE) and agar gel immunodiffusion (AGID). AGID test cannot be differentiated between RPV and PPRV but ICE and CIEP can be differentiated between these two viruses (Banyard, A.C et al, 2010).

PPRV REPLICATION AND LIFE CYCLE

Hemagglutination-neuraminidase (HN) protein found in Peste des Petits Ruminants Virus (PPRV) and sialic acid which is present in the host cell membrane responsible for first interaction of the host and pathogen. It was confirmed by the siRNA-mediated study that a putative co-receptor for PPRV might be signal lymphocyte activating molecules (SLAM. Neuraminidase is responsible for viral budding, which separates sialic acid residues from the carbohydrate moieties of glycoproteins. PPRV is distinctive in other morbilliviruses as in PPRV HN protein involves in both hemagglutination and neuraminidase actions, so it can be better termed as an HN protein in place of H protein (Munir M. et al, 2013).

VIRAL TRANSMISSIONS AND PROPAGATION

The virus can be spread from infected animals to the vulnerable animals by exhaled aerosol or clinical excretions .The virus is inactivated in a dry environment as it is a temperature sensitive virus. Infected animals that get rid from disease build up a protective immunity throughout their life and no carrier state has been recognized. Although, the virus can be found in animals body showing mild symptoms of disease resulting in disease outbreaks that subsequently affects the naive susceptible animals are. Age, sex, breed or seasons, which are other host factors, may also be part of the cause in disease development (Parida S. et al, 2015).

SIGN AND SYMPTOMS OF PPRV

Gastrointestinal tract and respiratory tract can be affected through PPR. Signs and symptoms of PPR included pyrexia, stomatitis, diarrhea, ulcerative lesions and oculo nasal discharge (Abubakar M. and Irfan M., 2014). Among the primary hosts for the virus, goats appear to be more prone to disease than sheep with some species of goat investigated to be more prone than others. The incubation period of the disease persist for 4–6 days, and it may go up to 3 to 14 days. Through the severe stage of disease, animals show high temperature (up to 41 °C) that might proceeds for 3-5 days and it could be follow malnutrition with distress. and dehydration. There is a discharge of mucus along with pus by watery nasal and lachrymal glands with extra saliva production. There is Necrosis of Erosive bruises in the oral cavity. In serious cases of illness, those bruises rise with the deposition of fibrin over the tongue. In late phases of the disease, there might be chances of cough, motion and abnormal breath. Lastly, the animal possibly will suffer from weight depletion, shortness of breath that eventually causes death (Parida S. et al, 2015).

OUTBREAKS OF PPRV

Four outbreaks of PPRV in Fars province of Iran were studied. Furthermore, the PPRV strains were isolated and analyzed phylogenetically. A total of 21 clinical samples were collected from oral, nasal, and ocular areas including blood sample also. Virus isolated in lamb kidney cell culture was identified through RT-PCR. Phylogenetical analysis revealed the resemblance of sequence with the virus isolated from Pakistan, Tajikistan and China. In contrast to other studies that showed similarity of sequenced N genes with the samples from Saudia Arabia. Sharing of common border could be a reason of similarity between Iranian and Pakistani strains of virus as there is frequent transboundry movement and trading of animals (Shahriari, R., 2019).

PPR infection was also appeared in Burundi and quickly proliferated in five provinces including Gitega, Kirundo, Mwaro, Muramvya and Karuzi. In Gitega, death of more than 4000 goats was estimated. Burundi government carried out investigation of outbreak initially in 2017. Lanzhou veterinary research institute provided cELISA in order to analyze 112 sera. About 37.5% sero positive results were obtained. Later on in 2018, further confirmation of the existence of PPR in Burundi was done by a joint investigation team of African Union Pan African Veterinary Vaccine Centre, African Interafrican Bureau for Union Animal Resources and East African Community. It was indicated phylogenetically that the virus were related to lineage III and found to be similar with the strains obtained from Kenya and Uganda in 2011 and 2012 respectively (Nivokwishimira, A. et al. 2019).

In literature outbreak of PPRV was also reported in Belbes city (Al-Sharkia governorate) in which 55 small ruminants suspected to PPRV infection were observed and studied. All those animals were freely move from one place to another and were not previously vaccinated. Conventional reverse transcription PCR was used to examine six tissue samples from oral lesions and four swabs sample from oculo-nasal cavity. The results indicated more sensitivity (100%) in comparison with virus isolation (70%). The PPRV strains identified and isolated were resemble with strains obtained from Ethopia (Elsheikh, H., et al, 2019).

Another study was conducted to insight an outbreak of PPRV in water deer found in Anhui province of China. The study confirmed the existence of PPRV infection in water deer, moreover also showed the presence of lineage II PPRVs that cause mortality of wild animals. The study suggested the government to focus the threat of PPRV infection in China (Zhou, X.Y. et al, 2018). In one of the study, mortality of more than 1000 wild goats and sheep was reported in the four provinces of Iran (central and northern) due to PPRV infection during 2014-2016. Similarity with the lineage IV strains has been revealed through partial nucleoprotein sequencing of 3 isolates of PPRV. The strains were found to be 99.4% identical with the PPRV-L4 strains that were common in northwestern and southeastern regions of China (Marashi, M., 2017). Another outbreak of PPRV reported the dissemination of PPRV in 22 provinces of China due to movement of animals. A total of 96 samples were collected from domestic ruminants and 13 samples from wild species including Capra ibex, argali and Goitered gazelle. PPRV was detected in 91 samples out of 96 samples while all the 13 samples were sero positive (Li.J. et al. 2017).

A study was conducted to highlight the sero prevalence of PPRV in domestic ruminants and camel in Sudan during the time period of 2008-2012. Serum samples (N= 12,384) were tested for the existence of PPR antibodies through competitive ELISA. The samples gathered from the Darfur states showed highest prevalence (68.1%) as compared to central states (54.3%). Samples of lung tissue (N=1276) were also collected and analyzed through immunocapture ELISA (ICELISA). A total of 233 (18.3%) samples showed positive results for PPR antigen. The prevalence of antigen was 33.6% in camel, 21.1% in goat, 15.4% in sheep and 12.3% in cattle. Isolation of virus was carried out in three different culture media including primary bovine, ovine kidney cells and vero cells. The PPR virus was isolated from 15 samples, out of 30 samples that were identified for the presence of virus using IcELISA (Intisar, K.S., 2017).

OUTBREAKS OF PPRV IN PAKISTAN

PPRV infection is prevalent in regions such as the Arabian Pennsylvania, the Middle East and in the Indian subcontinent (Abubakar et al, 2009). In this review, we considered the prevalence of virus in Pakistan. In 1994,Institute for Animal Health, Pirbright Laboratory, United Kingdom first recognized PPR in Pakistan. Few outbreaks have been registered while numerous outbreaks were happened since 1994. During the time span of 2002-2005, it was reported by the participatory disease surveillance team that the suspected incidences of PPR was 526. A total of 8,321 goats and sheep were influenced by these outbreaks. The team further reported that the occurrence of PPR outbreaks in many visited areas was associated with the incorporation of new animals in the flocks resulting in the spread of disease via communal grazing. These introductions of livestock were found to be more prevalent during an Islamic festival Eid-ul-Azha (Zahur A.B. 2008). One of the study revealed that the PPR antibodies were found to be more prevalent in sheep i.e. 54.09% while the seroprevalence in goats were found to be 44.15%. About 55.10% of sero-prevalence was observed in Sindh province that was highest among all the provinces (Abubakar et al, 2009). According to a study, out of 504 blood samples collected from sheep and goats of Punjab, PPR was identified in 79 blood samples. The area wise prevalence was found to be highest in Jhelum and Bahawalpur district i.e.21.2% as compared to Rawalpindi district i.e. 11.8% (Durrani A.Z., 2010). Similarly other outbreaks were also investigated in three commercial farms located in Taxila, Attock and Rawalpindi. A total of 116 animals showed symptoms of disease out of 365 animals. Within one to three weeks, the mortality rate was found to be 10-15% while the morbidity rate was 20-40% (Abubakar M. and Munir M., 2014). Another study reported the sero prevalence of PPR by conducting competitive-ELISA in samples collected from small ruminants of Sindh. A total of 35.23 % of sero prevalence was determined in ruminants. The rate of prevalence was found to be greater in females (35.94%) when compared with males (31.23%) (Nizamani A.R., 2015).

Another study was conducted to insight the occurrence of PPR outbreak due to the movement of PPRV-infected sheep and goats from the north -west of Sindh province to the central region of Punjab province. A total of 24 serum samples showed presence of PPRV antibodies out of 70 samples collected from 28 flocks using competitive ELISA. Moreover 18 samples of nasal swabs and feces showed positive result for PPRV antibodies. The gene sequencing differentiated both fusion and nucleoprotein gene into two groups. One group belongs to Pakistani isolates that are already recognized while the other group belongs to Middle East or Indian isolates (Munir M. et al, 2015).

In contrast to the above studies, one of the studies reported in 2016 revealed absence of PPRV antibodies in ruminants of Wildlife Park at Lahore and Faisalabad while anti-PPRV antibodies were detected in domestic small ruminants around these parks using competitive ELISA technique. Due to absence of PPR outbreak during the study period, N-gene based RT-PCR testing showed no existence of PPRV. It might be due to insufficient number of test samples collected from wildlife (Aziz-ul-Rahman et al, 2016).

Another study also investigated the existence of PPR infections in local small ruminants such as Kaili sheep and Beetal goats and also in imported ruminants including Dorper sheep and Australian Boer goat. The study indicated greater morbidity and mortality rate in local breeds of sheep and goats (Khan A. et al, 2018). Some other outbreaks of PPRV were also reported that affected 6221 animals. These outbreaks occurred during 2010 to 2013 and were investigated through molecular techniques. The number of outbreaks was found to be highest in province of Punjab. Out of 84 outbreaks, 38 outbreaks were reported from Punjab. A total of 48 outbreaks affected goats followed by 18 outbreaks in sheep while other outbreaks were found in mixed herds. Sheep were less seriously affected as compared to goats. In general, disease influenced each of the three groups however young animals were found more prone to the disease. All Pakistani strains clustered in lineage IV, PPRV irrespective of the gene whether F or N. Both cyclic and seasonal pattern of disease were observed through year wise information (Abubakar M. et al, 2018).

Recently in one of the study, occurrence of 20 outbreaks of PPR in 2016 was reported by collecting 20 swab samples from various areas including Islamabad, Rawalpindi, Abbottabad and Barnala, Azad Jammu & Kashmir. The study investigated the molecular as well as genetic nature of PPRV through phylogenetic analysis and it was suggested that the strains responsible for the outbreaks in Pakistan have resemblance with the strains identified from Iran and China. The analysis of nucleocapsid (N) gene further identified the presence of two different PPRV strains prevalent in Pakistan (Usman M. et al, 2019).

Another study reported 847 outbreaks of PPRV occurred in twenty six districts of Sindh and six districts of Karachi. During the year 2016, no outbreak was reported in Tando Mohammed Khan, Kandkote and Kambar Shahdadkot districts. Matiari district was identified with highest number of PPR disease outbreaks. The length of the outbreak was shortest i.e.5 days in Umerkot district while outbreak lasts long (62 days) in Larkana district. The study revealed the endemic condition of PPRV infection in the province. All the infected animals suffered with high fever (102.2 F-107.6 F), conjunctivitis, nasal and ocular discharges along with cough, diarrhea and mouth abrasions (Ali S.N. et al, 2019).

TREATMENT OF PPRV WITH PLANTS

There are some antiviral and some vaccines available to treat PPRV but herbal treatment is also an option for treating these diseases, for example goat weeds and ethno-veterinary herbal medicines. Some extracts of fruits like lemon give an effective treatment in contagious ecthyma. While goat weeds become activated against pyrexia. It is also used for dressing, used as laxative and also as purgative. If PPRV vaccine is not working alone then ethnoveterinary herbs should be used in combination with vaccine. This combination will be appeared more effective. Metabolite and extract of Ageratum convzoides Linn (Goat weed) have insecticidal and pharmacological actions. It is used in some diseases like in skin ulcers, against colic, febrifuge, antipyretic, and as purgative. Also used in cuts as dressing for wound. Neuromuscular action will be blocked by the crude extract of Ageratum conyzoidesLinn (Goat weed), this herb also healed up the wounds and provided analgesic efficacy. With ethanol goat weed provides protection against ulcer and spasmolytic effect. With oil goat weed provides anti inflammatory, analgesic and antipyretic effects. Similarly the metabolites of goat weed gives analgesic and antidepressant effects (Abubakar M. and Irfan M., 2014).

In a study Nigella sativa (N. sativa) with alcoholic extracts showed antiviral activity opposed to PPRV. This research reported that N. sativa (50 µg/ml) with alcoholic extract keep decreases the cytopathic effects of PPRV. This virus affected Vero cell lines and managed by six dilutions of N. sativa (200, 100, 50, 25, 12.5 and 6.25 µg/mL) with alcoholic extract. Mode of action was checked by Plaque reduction assay. Through 3-(4, 5)-dimethylthiahiazo (-z-5-di-phenytetra zolium romide v1)-3, colorimetric (MTT) assay, the antiviral efficacy was analyzed. From six dilutions, two dilutions of N. sativa (200 μ g/ml and 100 μ g/ml) extracts presented cytotoxicity to Vero cell lines. Cell survival was more than 50% in remaining three dilutions (50, 25, 12.5 µg/ml) and exhibit eloquent antiviral activity. In all the tested modes of action, alcoholic extracts of N. sativa (50 µg/ml) decreased the plaques count in contrast with the control negative (P < 0.05) in the plaque reduction assay (Aqil et al, 2018).

In another study, the leaves of babol Acacia Arabica. var. indica. locally known as babul (Mimosaceae) (BExt) were analyzed in Vero cell system for antiviral activity in peste des petits ruminants (PPRV). To describe the anti viral activity (non toxic concentration 150 and 200 µg/mL) against PPRV these assays are used: Virus titration, cvtopathic effect inhibition (CPE), sandwich ELISA (s-ELISA), PCR assays and cell ELISA. Viral infection was inhibited by BExt by decreasing antigen load and virus titer when pre incubated with virus before adsorption on cells or when added to post infection monolayers of cell. S-ELISA was used by using growth curve method, to analyze blocking of cell correlated and cell free PPRV at the time of replication when BExt was available in Vero cells. The dose of 200 µg/mL of BExt can be fully inhibited PPRV infection, and 150 to 200 µg/ml dose of BExt had virucidal effect. It showed that BExt inhibited release of virus and also inactivated the virus. The study showed that extract of A.arabica is a useful natural antiviral agent which can be used in PPR disease and it is an addition in phyto-anti viral repository for control of viral diseases. (Balamurugan V., et al 2008).

OIE (Office Internationale des Epizooties, World Organization of Animal Health) also suggested that infected or exposed animals should be decimated and remains should be buries or burned. It is also reported that, beside vaccination some general methods can be used including strict quarantine, sanitary prophylaxis, control of animal movement, and avoiding contacts with goats and sheep. Some ethnoveterinary treatment along with PPRV vaccine can be acceptable to treat disease (Dilli H.K., 2011).

Another study revealed that PPR is common in Indian subcontinent, Middle East and Africa. PPR is an endemic and intense illness of animals which can be produced by morbillivirus PPRV (Peste des petitsruminants virus). In major countries attenuated vaccine can be used which can be cured animals against PPR for three years. Despite, vaccine is not too much powerful against thermo tolerance. This study showed a hemagglutinin neuraminidase (HN), it is a protein of PPRV which found in plants of peanut (Arachis hypogea). It is found biologically active and it acquired neuro aminidase activity. Immunogenicity of HN protein which is derived from *Arachis hypogea* can be evaluated by oral immunization in sheep. Mostly HN protein of peanuts confined immune dominant epitopes in the natural arrangement of plant. Cell mediated immune response also found in sheep which are immunized through mucosa. When animals got oral immunization and no mucosal adjuvant was present, it showed response of antibody which neutralizes the virus (Khandelwal A., et al 2011).

In one of the study it is also reported that the antiviral activity of silver nano particles (SNPs) in contrast to PPRV, which is a Morbillivirus prototype virus. Argemonemaxicana is consumed as the reducing agent. The leaf extract of plant was consumed for compounding of biological SNPs from silver nitrate. SNPs are identified by applying UV through X-ray diffraction (XRD), transmission electron spectroscopy (TEM) and absorption spectroscopy. XRD examination explained the components, and TEM analysis explained the particle size of 5 to 30 nm of silver structure. Vero cells treatment with SNPs at non-lethal dose diminished the PPRV reproduction in vitro. It weakens the replication of PPRV at the time of entry of virus. TEM analysis exhibited SNPs collaborate with virion core and with virion surface. On the other hand this combination has no direct virucidal activity, but it produces an inhibiting effect on virus when it entered to target cells. It is the leading documented data which demonstrated that SNPs have ability to destroy the in-vitro replication of Morbillivirus (Khandelwal N., et al 2014).

In a study it was reported that, in worldwide PPRV ultimately affected the health condition of animals, which leads to a huge loss economically in flock of animals. PPRV is a virus which consists of one filament of RNA which produces Peste des petits ruminants (PPR). Acacia nilotica (Linn.) Delile is an important plant which is rich in tannis. It contains anti viral activity against many viruses which consist of single strand RNA. A.nilotica also used as food for animals and found throughout the subcontinent. In this research aqueous decoction of A. nilotica was used. Extract of leaves, bark and pods of plant used to describe antiviral activities and cytotoxic activity against PPRV. This research indicated that aqueous extract of bark did not exhibit any activity against viral infections, on the other hand aqueous extract of leaves of A.nilotica showed good result in contrast to extract of pods (Raheel R. et.al, 2013).

ATTENUATED AND RECOMBINANT SUBUNIT VACCINES

Recently, Nigeria 75/1 (lineage II) and Sungri 96 (lineage IV) attenuated vaccines are more commonly used while Arasur 87 is limited in India. Recombinant subunit vaccines have also been introduced. To ascertain their potency as well as duration of immunity. large scale testing of these recombinant vaccines are required (Parida S. et al. 2015). The main drawback of classical live attenuated vaccine is that antibody responses cannot be differentiated from naturally occurring infection. As a consequence, sero epidemiological surveillance of the disease is not feasible in the areas where vaccination program has alreadv been conducted (Balamurugan V. et al, 2014).

The vaccines were proved to be potent and are meant to contribute in long lasting immunity in both sheep and goats .Studies are conducted for improving the stability of PPR vaccines through temperature controlled vaccine and by using different other strategies. Research was conducted on synthetic short interfering RNAs (siRNAs) which causes preservation of serological status of animal by killing of virus (Kabir A. et al, 2019).

Vaccines nowadays used for PPRV possess cell cultured attenuated strains of PPRV that bring about same antibody outline as by natural infection. A vaccine that capable of differentiation of infected from vaccinated animals (DIVA) considered to be beneficial for control of PPRV and its eradication. A study was conducted to form a vaccine that is a DIVA vaccine which differentiates infected animals those that are vaccinated. from The immunogenicity of recombinant fowl pox (FP) and replication-defective recombinant human adenovirus 5 (Ad), expressing PPRV F and H proteins, in goats was assayed. The Ad brings about surpassing levels of virus precise and neutralizing antibodies and able larger numbers of CD8⁺ T cells than the FP-vectored vaccines. One dose of Ad-H having or not having additional Ad expressing ovine granulocyte macrophage colony-stimulating factor and/or ovine interleukin-2 boost up immunity as well as effectively secured goats from deadly PPRV after 4 months of vaccination (Herbert, R. et al, 2014).

CONCLUSION

This chapter highlights the use of different plants for the treatment of PPRV, still more

research is required in order to identify more plants for better results. Plants treatment are proved to be more economical for the treatment of PPRV but vaccines mention in the studies can be a gold standard for the complete eradication of PPRV in the whole region especially in those areas where PPRV is endemic.

FUTURE PROSPECTS

The outbreak of PPRV is being reported in almost each year in different countries including Pakistan. In some countries the facilities to identify and diagnosed the infection are available however developing countries are deprived of sophisticated labs in order to use diagnostic tool. Moreover some diagnostic kits are required that can be used in field conditions. In one of the study (Baron, M.D. 2017) Lateral flow device (pen side test) was mentioned that can identify the PPRV in the field and can prove to be an efficient tool in the absence of laboratory.

As in different studies it is revealed that there are many plants which lead to diminish the effect of PPRV. Beside plants research also has been conducted for vaccines and proved beneficial. In future more work can be performed on vaccine especially DIVA vaccine which differentiates infected from vaccinated one. These marker vaccines can prove to eradicate virus without making serological surveillance complication which may occur when other vaccination pathway is not different from infected pathway.

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