



ICPHS

Vaccines used in Echtyma disease and alternative treatment methods

Ektima hastalığında kullanılan aşılar ve alternatif tedavi metotları

Yakup Sinan ORTA¹, Kamil ATLI¹, Mehmet KALE¹,

¹Burdur Mehmet Akif Ersoy University, Faculty of Veterinary Medicine, Department of Virology, Burdur, Türkiye.

CURRENT PERSPECTIVES ON

HEALTH SCIENCES

Received 12.07.2022 Accepted 04.09.2022 Published Online 30.09.2022 Article Code CPHS2022-3(2)-5

Abstract

Ecthyma is a worldwide zoonotic disease with a significant morbidity rate among sheep and goats, which leading to yield losses. Orf virus (ORFV), the cause of ecthyma, is in the parapoxvirus genus, subfamily Chordopoxvirinae and family Poxviridae. ORFV enters the living body through damaged tissues and multiplies in epidermal cells. Ecthyma is usually transmitted to healthy animals by contact from infected animals. Disease can be observed experimentally or naturally in wild and domestic animal species such as camel, alpaca, squirrel, seal, reindeer, musk ox, mule deer, white-tailed deer, antelope, roe deer, and wildebeest. Although ORFV is endemic in many countries, it is not included in the status of a notifiable disease by OIE (Office International des Épizooties). However, ORFV is recognized by the OIE as a zoonotic disease and produces limited localized pustular lesions, usually on the hands of humans. This disease has a mortality rate of 10-90% in lambs and kids, while it has a low mortality rate in adult sheep and goats. Mortality rate increases because of lambs and kids do not suckle their mothers and secondary bacterial infections. Peste des petits ruminants virus (PPRV), caprine papillomavirus (CaPV), mycoplasma, streptococcus, staphylococcus agents can also be seen together with ORFV. This disease, which can be seen periodically in small cattle, has recently been seen in every period of the year, resulting in the need to develop new approaches in the treatment of the disease. In this review, detailed information was given about the vaccines and alternative treatment methods that are widely used all over the world in the protection and treatment of ORFV, induced ecthyma in sheep and goats.

Öz

Ektima, dünya çapında koyun ve keçilerde arasında önemli morbidite oranına sahip, verim kayıplarına yol açan ve zoonotik bir hastalıktır. Ektima hastalığının etkeni Orf virus (ORFV); Parapoxvirus genusu, Chordopoxvirinae alt ailesi ve Poxviridae ailesi içerisinde yer almaktadır. ORFV canlı vücuduna hasar gören dokular aracılığıyla girer ve epidermal hücrelerde çoğalır. Ektima sağlıklı hayvanlara genellikle enfekte hayvanlardan temas yoluyla bulaşmaktadır. Hastalık; deve, alpaka, sincap, fok, ren geyiği, misk sığırı, katır geyiği, beyaz kuyruklu geyik, antilop, karaca, kara antilopu gibi vahşi ve evcil hayvan türlerinde deneysel veya doğal olarak görülebilmektedir. ORFV birçok ülkede endemik olmasına rağmen OIE (Office International des Épizooties) tarafından ihbari mecburi hastalık statüsünde yer almamaktadır. Ancak ORFV, OIE tarafından zoonotik bir hastalık olarak kabul edilmektedir ve insanların genellikle ellerinde sınırlı lokalize püstüler lezyonlar meydana getirmektedir. Bu hastalık, kuzu ve oğlaklarda %10-90 arasında mortalite oranına sahipken, yetişkin koyun ve keçilerde düşük mortalite seyirlidir. Bunun nedeni kuzu ve oğlakların annelerini emmemeleri ve sekonder bakteriyel enfeksiyonlardır. ORFV ile birlikte koyun keçi vebası virusu (PPRV), caprine papillomavirus (CaPV), mikoplazma, streptokok, stafilokok etkenleri de birlikte görülebilmektedir. Küçükbaş hayvanlarda dönemsel olarak görülebilen bu hastalığın son zamanlarda yılın her döneminde görülmesi sonucu hastalığın tedavisinde yeni yaklaşımlar geliştirilmesi ihtiyacı doğmuştur. Bu derlemede, koyun ve keçilerde ORFV kaynaklı ektima hastalığından korumada tüm dünyada yaygın olarak kullanılan aşılar ve alternatif tedavi metotları hakkında detaylı olarak bilgilendirme yapılmıştır.

Keywords

ecthyma treatment vaccine alternative methods

Anahtar kelimeler ektima tedavi aşı alternatif yöntemler

Corresponding Author Mehmet KALE drmkalex@yahoo.com

ORCID YS Orta 0000-0002-6918-4819

K Atlı 0000-0002-2266-4372

M Kale 0000-0003-4156-1077

To cite this article:

Orta YK, Atlu K, Kale M. Vaccines used in Echtyma disease and alternative treatment methods. Curr Perspect Health Sci, 2022;3(2): 82-91

INTRODUCTION

Echtyma, also called infectious pustular dermatitis, is usually seen in young goats and sheep and is an acute, contagious and zoonotic viral skin disease which might cause economical losses (1). Goats are more sensitive compared to sheep and the disease progresses more slowly. Echtyma mostly appears with proliferative lesions and lesions disappear in 1 or 2 months (2). Lesions inside and around mouth prevent lambs and yeanlings from sucking while lesions in teats inhibit feeding of babies. Lesions which might occur on legs may cause temporary limping. The infection is repetitive and lesions proceed within the same clinical phases but their size is smaller. Echtyma is not a fatal disease under normal conditions; however, it is a weakening disease that might cause deaths in terms of preventing lambs and yeanlings from sucking and forming secondary bacterial or fungal infections (3). Morbidity in echtyma is as high as 100% and mortality may reach up to 15% depending on secondary infections (4). Vaccination is the most commonly preferred method in disease treatment. However, alternative treatment methods are also used since vaccines are produced in limited amount and their immunity has a short-term effect.

Commercial ORFV Vaccines Produced in Turkey

Dermavac[™] ecthyma vaccine

Dermavac[™] vaccine is produced by Vetal Inc. located within the borders of Adıyaman province in our country. The product is a lyophilised, live attenuated vaccine prepared in calf kidney cell cultures. The vaccine is applied in order to protect lambs and yeanlings against echtyma disease. The vaccine is injected in scarification as deep enough to pass through the initial layer of the skin but not to cause bleeding in crossways of 3-4 lines with a length of 0.5-1 cm. collectively in Regio Inguinale region (inner part of back leg) for lambs and yeanlings of all ages after births are completed for protection and on areas where the disease is seen right after birth. The vaccine is applied by dropping here 2-3 drops from the dropper and waiting for a few seconds. The vaccine is applied as a protector on areas where the disease is seen and areas where the disease was previously seen. No vaccine is applied on areas with no disease. Immunity is formed fully in 21 days and lasts for 6 months (5).

Penorf vaccine (Pendik Veterinary Control and Research Institute)

Penorf echtyma is a lyophilized, live attenuated vaccine prepared for protecting lambs and yeanlings against echtyma disease. The composition of the vaccine includes 1 ml 102.6 DKID50, Lactalbumin hydrolysate 0,000375 mg and Sucrose 0,00075 mg. The vaccine is applied collectively for lambs and yeanlings of all ages on areas where the disease is seen right after birth and for protection after births are completed. The immunity period of the vaccine is one year (6).

Orfdoll vaccine

ORFDOLL vaccine is used against echtyma disease which causes infections in mouth, lips, eyes and skin in sheep, goats, lambs and yeanlings. This vaccine is produced in production facilities of Dollvet Inc. in Şanlıurfa province. The vaccine is applied on all lambs and yeanlings from the age of one and sheep and goats of all ages. Since the immunity period of the vaccine is maximum 12 months, animals need to be vaccinated at the same dose each year. 28 days before or after the application of the vaccine, corticosteroids or immune suppressive drugs are not recommended to be used (7).

Commercial ORFV Vaccines Produced Around The World

Ovine ecthyma vaccine

This product is a live vaccine prepared as lyophilized for sheep and goats and produced by American Colorado State Company. It includes penicillin and streptomycin as preservatives. It is recommended for vaccination of both sheep and goats against sore mouth infections caused by sheep echtyma virus. Each newborn lamb and yeanling are recommended to be vaccinated. In order to prevent the disease from spreading, animals are recommended to be vaccinated at least ten days before shipment. Normally, only healthy animals should be vaccinated. However, research showed that vaccination of infected sheep and goats during sore mouth epidemics shortens the course of the disease. The packet includes needle applicators provided with the vaccine. Thanks to this applicator, the outer layer of the skin could be scratched without bleeding and one drop of the vaccine could be dropped onto at least 1 square inch (0.04 ml) of an area. No vaccination is recommended within 21 days before slaughtering (8).

Ovine ecthyma vaccine

This product is a lyophilized live vaccine prepared for those symptoms developed as sore mouth in sheep and goats. This commercial vaccine has been improved by Texas A&M AgriLife Extension and Bimeda Biologicals since 2015. It has been reported that the vaccine is prepared by using scabs collected from mouth areas of infected animals and live experimental animals with no virus history previously are controlled. The vaccine is originally produced from ORFV 47CE strain isolated under lab conditions during an epidemic seen in goats (9). In order to protect lambs, the vaccine is declared to be used by putting a scratch on inner thigh area and glycerin bottles are used to spread the vaccine in the area. No vaccination is recommended 21 days before slaughtering. This product is 100dose and includes 60-70 mg live virus and 6-7 ml. sterile diluent fluid. The vaccine is recommended to be applied on healthy lambs. The protection period of the vaccine has not been reported (10).

Scabivax[®] Forte

Scabivax[®] Forte is a live vaccine providing active immunization against clinical symptoms caused by ORFV in sheep and lambs. It has been improved by a company called MSD Animal Health. Immunization occurs in 4-8 weeks following the vaccination. It provides protection for 12 months against symptoms of common contagious pustular dermatitis. The pregnant are recommended to be vaccinated 7 weeks before lambing. Lambs can be vaccinated right after birth. The vaccine is produced from live ORFV New Zealand NZ2 strain (11). The dose of the vaccine is prepared as Orf virus 105.4-106.5 DKID50. The vaccine contains Patent Blue V (E 131), HEPES buffer, Sodium hydrogen carbonate, Eagles Minimum essential medium with non-essential amino acid, Foetal bovine serum, NZ Amine type B, Sucrose, Gelatin, Glutamin, Glycerol and Injection fluid. No preservatives have been used within the vaccine (12).

ORFV D1701 live vaccine

ORFV D1701 is a high attenuated strain licensed in Germany as a live vaccine used against contagious echtyma disease in sheep. The virus has originally been isolated from sheep and its pathogenity has been decreased following serial passages. Virus attenuation in sheep has been reported as deletion of three genomic areas of ORFV D1701 strain to be adapted into vero cell culture. This vaccine is the most reliable one amongst those used on our day due to the fact that it has been prepared in Vero-cell, it has a low pathogenity and it is easy to produce. Following the vaccine application after scratching, medium level lesions develop and they provide immunity for 4-6 months (13).

Various Experimental Vaccine Studies and Patented ORFV Vaccines

Many experimental vaccine studies have been carried out for echtyma disease caused by ORFV for many previous years. These studies are still performed today. In the study, Ramyar (14) studied with four local strains from Iran and two strains from Germany Munich University Animal Diseases Microbiology Institute. These strains were adapted into cell culture and kept under -30oC after lyophilisation. When preparing the cells, Hanks solution and serum (10%) including 0.5% lactalbumin hydrolysate was used. Nodules appearing on the vaccinated area disappeared in 7-10 days and animals were provided with immunization. Gallina et al. (15) prepared a subunit vaccine with cloning and expression of ORFV FL1 gene. After vaccination, they showed that F1L proteins in rabbits might stimulate the production of neutralized antibodies. Musser et al. (9) carried out an effective vaccination practice towards echtyma virus strains in goats. In the study, five strains were selected as to be the best seed strains of echtyma vaccine. Medium level common scabbing was detected in two of the strains following the infection and goats were stated to have been protected in the other three strains following the vaccination. In this study, 47CE strain has been selected as the main seed source in producing echtyma vaccine. This strain has been reported to be protective for all the yeanlings. Schmidt et al. (16) subpassed ORFV IA-82 strain (106.9 DKID50/ml) in BHK-21 cell for 21 times and they carried out this practice by scarifying the skin in the inner surface of the back legs of 30 lambs. Pustule and scabbing were seen in 16 of 30 animals following the vaccination. After this experimental study, cell culture-based ORFV vaccines were reported to have provided partial immunization and protection. Mercante et al. (17) attenuated a wild ORFV strain within primer chicken embryo fibroblast cell culture at the end of serial passages. They detected 104.5 DKID50 titre in 1 ml. dose vaccine content. As a result of applying the vaccine on sheep and lambs intramuscularly (i.m.), no echtyma lesions were seen on animals and symptoms of disease appeared and continued on control group animals.

Abousenna et al. (18) carried out a study in order to adapt echtyma vaccine strain into MDBK cell culture and to detect the shelf life, stability and immunity level of echtyma vaccine produced in MDBK cell culture in sheep. In the study, they found the titre of the vaccine virus adapted into MDBK cell culture as DKID50 106.5/ml. On the 30th day following the vaccination, they detected neutralizing antibodies in blood serum collected from lambs and vaccinated lambs were protected against echtyma infection as a result of a challenge performed with pathogen echtyma virus. During stability studies, lyophilised vaccine titres kept for 24 months under +4/+80C were found as favourable ones between 1st and 24th months.

Some of the vaccine practices on echtyma disease caused by ORFV have been secured by patent. Anton (19) developed a patented methodology about preparing and parenteral usage of live vaccines against ORFV infection in sheep and goats. Within this methodology, they adapted ORFV D1705 attenuated strain into embryonic cattle lung cell culture and recommended to perform parenteral vaccination twice against ORFV infection in sheep and goats. Inst. Biokhim Fiziol Academy N (20) developed a live cell culture vaccine against echtyma disease. For this purpose, primer skin cell culture of sheep, medium 199, 2% cattle serum and L-1 virus strain were used. The basic purpose of the vaccine is the live cell culture vaccine prepared against echtyma disease seen in sheep, calves and other animals. Khanduev et al. (21) got patent by developing a live vaccine following subpass and attenuation from foetus skin of lambs in France. Primer cultures of sheep foetal skin cells were used. N199 medium and 2% cattle serum was used in order for cells to grow. L1 attenuated viral strain was subpassed between 10-20 in these cell cultures. The basic purpose of the vaccine is to provide immunity for at least 9 months with attenuated strain in sheep in case of epidemic echtyma. Lanzhou Veterinary Research Institute of CAAS (22) in China developed a patented attenuated echtyma vaccine. MDBK cell culture ORFV HB-TS09 strain was used for the vaccine. The basic purpose of the vaccine is to weaken the virus in cells in infective pustules and to set and perform this as a preparation method. Lanzhou Veterinary Research Institute of CAAS (23) in China developed a patented goatpox virus and ORFV combined cellbased attenuated vaccine. While preparing the vaccine, newborn cattle primer testicle cell culture, newborn Testis Caprae seu Ovis primer cell cultures, Dulbecco's Modified Eagle Medium (DMEM) medium, ORFV HB-TS09F65 and goatpox virus HN-XY2010F43 strains were used. Lanzhou Veterinary Research Institute of CAAS

(24) in China developed a triple cell-based attenuated vaccine for goatpox, sheeppox and aphtovirus. In the study, DMEM was used for producing lamb testicle cell cultures. HN-XY2010F43 strain was used as goatpox virus, GS-WW2010F44 strain as sheeppox virus and ORFV HB-TS09F65 strain for sheep infective pustule virus. The main purpose of the vaccine is live attenuated vaccines developed against all three viruses for protection and controlling. Lanzhou Veterinary Research Institute of CAAS (25) in China developed a patented sheeppox and orf bivalent cell-based attenuated vaccine. They used newborn cattle testicle cell culture and lamb testicle cell culture line for producing the vaccine, DMEM medium for cell production and ORFV HB-TS09F65 and sheeppox virus GS-WW 2010F44 strains for preparing the viral antigen. The main purpose of the vaccine is to avoid sheeppox and sheep aft and to control them. Lanzhou Veterinary Research Institute of CAAS (26) in China found patented echtyma virus (soremouth) recombinant protein antigen vaccine. For this purpose, echtyma virus EEV cyst membrane ORF059 recombinant protein, IMV ORF047 recombinant protein and adjuvant (ISA201) were used. As a result of mixing these two kinds of recombinant protein antigens, the vaccine could be provided with both cellular immunity and humoral immunity.

The New ORFV Vaccines Being Developed

Great success has been achieved so far in developing vaccines. The improvements in the field of DNA vaccines will be able to play a crucial key role in developing ORFV vaccines. Future vaccine design technologies should focus on obtaining the desired potential immune responses against antigens (27,28). Effectiveness/safety, adjuvants and delivery system strategies need to be increased for improving new vaccines about ORFV vaccines (29,30). Vaccine platforms, relation between dense vaccine applications, costs and transport of the products produced at a great scale and reliability, effect and strength of the vaccine have been focused on greatly. The vaccines planned to be produced for ORFV infections in the future are nano particle-based subunit and peptide vaccines, DNA vaccines and parapox vector vaccines. Arrival of these kinds of vaccines makes us to consider developing them so as to limit their usage owing to the fact that attenuated virus vaccines could easily be virulent (27,28).

Subunit and peptide vaccines should be prepared from either glycoproteins or proteins obtained from specific ORFV gene in order to achieve a strong immunity (31).

In addition, subunit and peptide vaccines can be produced safely and easily when compared to conventional live vaccines and inactive ones in terms of effectiveness (32). It is a pity that adjuvants are needed to increase immunity since subunit vaccines provide short term immunity (33). Today, as a result of improvements in the field of nanotechnology, nanoparticles make it possible to increase cellular immune response when specific viral antigens reach the target cell (34). Therefore, as the present immunogenicity improves, nano-adjuvant vaccines will be used in future vaccine candidates (35). Peptide, subunit and inactive vaccines are highly reliable; however, they create lower immunogenicity compared to live attenuated viral vaccines (31). That's why vaccine candidates with low immunogenicity like these should be supported by substances stimulating immune response such as nanoadjuvants (36). In this regard, nano-adjuvants should follow the paths used in vaccine development. These can be identified as increasing vaccine antigen effectiveness, binding or oscillation of vaccine antigens onto target cells continuously, protection of vaccine antigens being used as far as possible, decreasing the amount of vaccine antigen (dose) to be used for reducing the production cost for vaccines to low levels, antibody specifity and affinity, increasing avidity and accelerating distribution of antigens into target cells (33). Nanoparticles are easily absorbed by antigen offering cells due to their structure and shape, and especially dendritic cells and lymph nodules, humoral cells make it possible by stimulating immunity (37). Therefore, nano-adjuvants will be used in the future for both effectiveness and increase the effects of vaccines. If nanoparticle-based vaccines do really good, they should play an important role in detecting control strategies in ORFV infections in the future (30).

Peptide vaccines are subtype of subunit vaccines. They are synthesized peptides including immunogenic particles of target virus immune dominant proteins in vitro (30). However, peptide-based vaccines are easily produced and have a much higher stability than subunit vaccines do (all proteins). What is more interesting is that peptide vaccines are more advantageous than subunit ones in terms of low antigen amount, low toxicity and low production costs (38). In peptidebased viral vaccines, immunogenicity increases due to the effectiveness of immune adjuvants (T cell response CD4+ and CD8+) and humoral immune response (IFN-). Today no peptide vaccine developed against ORFV and other viral infections has yet been produced. However, influenza virus and human papilloma virus peptide-based vaccines have been reported to create the

desired immune response (39). Interestingly, peptide vaccines are among the future candidate vaccines since they are easily synthesized, stable and highly reliable in hosts where the vaccine is applied (38).

Recombinant viral vector vaccines are the engineering vaccines in which vaccine antigens are formed via vectors. Adenovirus, flavivirus, herpesvirus, Newcastle disease virus, parvovirus and poxviruses are among the viral vector vaccines commonly used on our day (40). ORFV vector vaccines provide T cells and humoral immune response while lacking of systemic distribution of the virus and limited host target causes a disadvantage. These vaccines are competitors of traditional conventional vaccines (41). In a study carried out on animals recently, recombinant vaccines have been reported to stimulate humoral and cellular immune response (29). Vector vaccines are both replications and combined versions of non-replication subunit vaccines (42). However, developing such vaccines is highly complex and expensive (43).

Alternative Treatment Methods

Many alternative methods have been used for echtyma disease developing in animals due to ORFV. Bita et al. (44) used three formulations for echtyma disease seen in sheep and goats grown for milk production. Formulation 1: Methylene blue+oxytetracycline powder+honey/vaseline; formulation 2: Methylene blue+oxytetracycline powder+osmatin; formulation 3: Methylene blue+oxytetracycline powder+grease oil. 90% healing was obtained by using these treatment formulas for five days.

Brahma et al. (45) used potassium permanganate to clean nose, lip and inner mouth lesions developed due to ORFV in three 6-month-old goats and applied 5 ml/ kg enrofloxacin, 0,5 mg/kg meloxicam and 0.5 mg/kg chlorpheniramine maleate intramuscularly. They also applied a mixture of aloe vera gel and turmeric powder twice upon lesions. After a week, lesions from ORFV completely disappeared.

In lesions from ORFV observed in mouth and inner mouth mucosa seen in two lambs among Irish sheep, Onyango et al. (46) applied 200 mg/kg procaine penicillin, 250 mg/kg dihydrostreptomicin sulphate and 1.5 petroleum-based pentanediol softening pomade on both lambs for 3 days. They stated that the treatment achieved successful results.

Chauhan et al. (47) used cephalosporin group antibiotics against secondary bacterial infections, meloxicam anti-inflammatory medicine, as pheniramine maleate as antihistaminic and vitamin B and C complexes and wide spectrum tropical pomade as supportive treatment for lesions due to ORFV seen on head and nasal areas of a 2.5-month-old yeanling and detected a clinical recovery in two weeks. Dar et al. (48) performed different treatment methods in three different groups (24 animals in each group) for a herd with echtyma including 72 animals, of which 53 were sheep and 19 were goats. They obtained 100% recovery in group 1 by applying enrofloxacin+boroglicerine pomade, 100% recovery in group 2 by applying oxytetracycline+topical antibacterial pomade and 79% recovery in group 3 by applying povidoneiodine+antibiotic+cortizone pomade. At the end of the study, in sheep and goat herds in which echtyma disease was seen, using parentarel antibiotics together with topical antiseptics proved to be highly effective. Lacasta et al. (49) obtained successful results in the early stages of the disease using a commercial product prepared as gel called Tri-Solfen® which they developed for ORFV lesions seen in one-month-old lambs. This commercial product contains two local anaesthetics (Lignocaine and bupivacaine), adrenalin and antiseptic (cetrimide).

Cidofovir (HPMPC, CDV, Vistide) has an effective activity against a wide DNA virus scale including poxvirus (50). During in vivo studies on experimental infected lambs, Cidofovir proved to provide quite fast results in medium level echtyma lesions (51). Cidofovir has an important role in decreasing live viruses in lesions and decreasing disease incidence in herds persisted by ORFV (52). On our day, Cidofovir/ Sucralfate gels are used in spray formulations for ORFV-infected lambs. These gels are active against the virus and are used for treatment of many animals under field conditions (53).

In order to treat and protect sheep and goats from ORFV infections, traditional and alternative methods are also available. Various oils (sesame and castor oil) such as Sodom apple juice (Calotropis procera) and euphorbia (Euphorbia spp.) are used in some African countries (54).

The plant called ilex (Ilex aquifolium) is used in Holland and France in treatment and protection from echtyma disease (55).

In recent years, Papilend[®],[™] wart pomade has been reported to provide successful results in echtyma cases seen in lambs, yeanlings, sheep and goats.

(Prof.Dr.Mehmet Kale, 2022, Personal Contact info). This product contains glacial acetic acid, salicyclic acid, garlic oil, tea tree oil, glyceryl mono stearate, stearic acid, cetyl stearyl alcohol, hydrogenized castor oil, podophyllum and water. As for how to use the product and the amount of dosage, it is applied onto wart formations or their roots once in the morning and once in the evening (56).

Liu et al. (57) applied ozone oil on 121 Korean native goats infected with echtyma daily for 30 days. In the study, 200 ppm. ozone gas was added into drinking water for an hour. This ozone water (0.1 ppm.) was given to infected animals as ad libitum. Ozone therapy became successful in all the goats with echtyma lesions.

Sunitha et al. (58) applied a treatment procedure on 15 yeanlings with inner mouth, nose and lip ecthyma lesions. Within this procedure, animals showed full recovery in two weeks as a result of using potassium permanganate solution, bead tree leaves, turmeric, lemon juice and salt combinations for at least twice each day.

Wang et al. (59) recommended using drugs such as Zylexis supporting immune system in order to reduce the pressure on immune system (especially due to stress) that occurs when ORFV infections appear in animals.

In recent years, developing and supporting veterinary applications has been considered greatly owing to reasons such as treatment difficulties in echtyma, sheep/goat plague and footrot diseases commonly seen in goat farms, alternative treatment search, obtaining medical plants easily and costs (60).

CONCLUSIONS

Vaccination is an effective and cost-effective method in preventing ORFV infections. Transposition is recommended as ORFV is carried over barns (feeders, drinkers, building, floor and environment) in herds having echtyma disease each year even though vaccination, disinfection and supportive treatment is provided. Isolation of infected animals might help prevent the disease from spreading. In order to stop Orf virus from entering, new animals should be taken under quarantine before assembling with the other animals of a farm. Some healthy-looking vector animals with no disease symptom may spread the virus. Necessary precautions must be taken to prevent the virus from spreading around the farm via the equipment and other fomites. Especially during spring, spreading of echtyma disease in herds is a predisposed factor due to formations of mouth and lip injuries in sheep and goats fed with thorn plants such as ryegrass. In such cases, mouth and lip injuries of animals should be treated with antiseptics frequently. Besides, transporting animals, especially infected ones, from one place to another should be prohibited. Infected babies, teats of sheep that are susceptible to infections and echtyma lesions in mature ones might cause the virus to spread in herds. Therefore, newly developing lesions in early stages of the disease should be intervened. Injuries in mouths of the babies greatly limit feeding and as a result lambs cannot get the colostrum's necessary for immunity. This in turn causes lambs to die or to catch diseases frequently in their later life even though they survive. Non-complicated cases heal by themselves in 4-5 weeks without treatment. In case of secondary bacterial infections or worm invasion, animals might die at a rate of 10-50%. Antiseptics, antibiotics and antiparasitaries are recommended to be used for such lesions. As precaution, fly spray/ traps might help limit worm invasion. Since echtyma disease formed by ORFV may be seen in all climate conditions, the disease may easily spread and cause frequent epidemics. Today, the disease based on global warming may be seen in almost all seasons. Lesions developing as a result of echtyma might be confused with capripox, blue tongue, cattle plague, dermaphiliosis and mange. Therefore, they should be distinguished with tests applied on a molecular level. Vaccination is the most basic protection method in echtyma disease, however, short term immunity of vaccines and repeating the vaccine each year is an important disadvantage. Therefore, during the early stages of the disease, using alternative treatment methods might prevent the disease from spreading within the herd. Alternative treatment products developed for echtyma disease by various researchers in recent years have also been considered as important. Therefore, studies aiming to develop new commercial products in this field should be supported.

Conflict of interest/Çıkar çatışması: In terms of this study, authors and/or family members have no medical committee membership or relations with members, consultancy, expertness, employment in any companies, shareholding and similar conditions that could cause potential conflict of interests.

Author contributions: Study design: YSO, KA, MK; Literature review: YSO; Draft preparation: YSO,KA; Critical review for content: YSO,KA, MK; Final approval of the version to be published: KA, MK.

REFERENCES

1. Mondal B, Bera AK, Hosamani M, Tembhurne PA, Bandyopadhyay SK. Detection of orf virus from an outbreak in goats and its genetic relation with other parapoxviruses. Vet Res Commun. 2006;30:531–9.

2. McKeever D, Jenkinson DM, Hutchison G, Reid H. Studies of the pathogenesis of orf virus infection in sheep. J Comp Pathol. 1988;99:317–28.

3. Haig DM, McInnes CJ. Immunity and counter immunity during infection with the parapoxvirus orf virus. Virus Res 2002;88:3–16.

4. Gumbrell RC, McGregor DA. Outbreak of severe fatal orf in lambs. Vet Rec. 1997;141:150-1.

5. Vetal Dermavac. SearchEngineWatch Web site. https://vetal.com.tr/dermavac. Accessed April 19, 2022.

6. T.C. Tarım ve Orman Bakanlığı İstanbul Pendik Veteriner Kontrol Enstitüsü. Penorf Aşısı (Ektima). SearchEngineWatch Web site https://vetkontrol. tarimorman.gov.tr/pendik/Menu/18/Urunlerimiz. Accessed April 19, 2022.

7. Dollvet. Orfdoll Canlı Ektima Aşısı. SearchEngineWatch Web https://dollvet.com.tr/ urunler/orfdoll/. Accessed April 19, 2022.

8. Colorado Serum Company. Ovine Ecthyma Vaccine. SearchEngineWatch Web https://coloradoserum-com.3dcartstores.com/ovine-ecthyma. Accessed April 19, 2022.

9. Musser JMB, Taylor CA, Guo J, Tizard IR, Walker JW. Development of a contagious ecthyma vaccine for goats. Am J Vet Res. 2008;69:1366–70.

10. Bimeda Biologicals. Ovine Ecthyma Vaccine. SearchEngineWatch Web https://www. bimedabiologicals.com/products/sheep-vaccines. Accessed April 19, 2022.

11. Hosamani M, Scagliarini A, Bhanuprakash V, McInnes CJ, Singh RK. Orf: an update on current research and future perspectives. Expert Rev Anti Infect Ther 2009;7:879-93.

12. NOAH Compendium. Scabivax[®] Forte. SearchEngineWatch Web https://www. noahcompendium.co.uk/?id=-456135. Accessed April 19, 2022. 13. Rziha HJ, Henkel M, Cottone R, Bauer B, Auge U, Götz F, et al. Generation of recombinant parapoxviruses: non-essential genes suitable for insertion and expression of foreign genes. J Biotechnol. 2000;83:137-45.

14. Ramyar H. Etude sur la possibilité du contrôle de l'ecthyma contagieux a l'aide d'un virus vaccin préparé sur cultures cellulaires. Arch Razi Inst. 1973;25:5-7.

15. Gallina L, Scagliarini A, Ciulli S, Prosperi S. Cloning and expression of Orf virus F1L gene: possible use as subunit vaccine. Vet Res Commun. 2004;1:291-93.

16. Schmidt C, Cargnelutt, JF, Martins M, Weiblen R, Flores, EF. Vacina experimental produzida em cultivo celular confere proteção parcial contra o ectima contagioso em ovinos. Pesqui Vet Bras. 2012;32:11-6.

17. Mercante MT, Lelli R, Ronchi GF, Pini, A. Production and efficacy of an attenuated live vaccine against contagious ovine ecthyma. Vet Ital. 2008;44:543-7.

18. Abousenna MS, Amal AM, Aziz HA, Barghooth WM, Shafik NG. Determination of the effect of ecthyma vaccine virus on immunity against the foot and mouth disease (fmd) vaccine in sheep. J Anim Health Prod. 2020;8:19-26.

19. Anton M (1981). Orf virus, process for the preparation of an orf virus live vaccine and its use for parenteral protective inoculation against orf infections in sheep and goats. SearchEngineWatch Web https://patents.google.com/patent/DE3136430A1. Accessed April 19, 2022.

20. Inst Biokhim Fiziol Akademii N (1981). Live virus cultural vaccine against contagious ecthyma and method for preparing same. SearchEngineWatch Web https://patents.google.com/patent/GB2097671A. Accessed April 19, 2022.

21. Khanduev TT, Imanov ED, Gusev BN, Sultanov TS, Makarova EV, Salidinov B, Chormonova NB (1981). Live vaccine against contagious ecthyma of sheep-prepd. from virus attenuated by passaging on foetal skin cells. SearchEngineWatch Web https:// patents.google.com/patent/FR2499411A1. Accessed April 19, 2022.

22. Lanzhou Veterinary Research Institute of CAAS (2014). Attenuated vaccine of contagious ecthyma virocyte as well as preparation method and application thereof. SearchEngineWatch Web https://patents. google.com/patent/CN104017776A. Accessed April 19, 2022.

23. Lanzhou Veterinary Research Institute of CAAS (2015). Goatpox virus-orf virus combined cell attenuated vaccine and its preparation method and use. SearchEngineWatch Web https://patents.google. com/patent/CN104758928A. Accessed April 19, 2022.

24. Lanzhou Veterinary Research Institute of CAAS (2016a). Goat pox, sheep pox and aphtha triple cell attenuated vaccine and preparation method and application thereof. SearchEngineWatch Web https://patents.google.com/patent/CN106075429B/. Accessed April 19, 2022.

25. Lanzhou Veterinary Research Institute of CAAS (2016b). Sheep pox and orf bivalent cell attenuated vaccine and preparation method and application thereof. SearchEngineWatch Web https://patents. google.com/patent/CN106139141B/ Accessed April 19, 2022.

26. Lanzhou Veterinary Research Institute of CAAS (2016c). A kind of sore mouth virus recombinant protein antigen vaccine and preparation method thereof. SearchEngineWatch Web https://patents. google.com/patent/CN105727278B/ Accessed April 19, 2022.

27. Dalal A, Kumar V, Chaudhary D, Bansal N, Kumar A, Kakker N, et al. Past and present overview of "Orf." Int J Curr Microbiol Appl Sci. 2017;6:2159–73.

28. Shimizu K, Takaiwa A, Takeshima SN, Okada A, Inoshima Y. Genetic variability of 30-proximal region of genomes of orf viruses isolated from sheep and wild japanese serows (Capricornis crispus) in Japan. Front Vet Sci. 2020;7:1–7.

29. Vetter V, Denizer G, Friedland LR, Krishnan J, Shapiro M. Understanding modern-day vaccines: What you need to know. Ann Med. 2018;50:110–20.

30. Bull JJ, Nuismer SL, Antia R. Recombinant vector vaccine evolution. PLoS Comput Biol. 2019;15:e1006857.

31. Baron MD, Iqbal M, Nair V. Recent advances in viral vectors in veterinary vaccinology. Curr Opin Virol. 2018;29:1–7.

32. Yogisharadhya R, Kumar A, Bhanuprakash V, Shivachandra SB. Evaluation of a recombinant major envelope protein (F1L) based indirect—ELISA for sero-diagnosis of orf in sheep and goats. J Virol Methods. 2018;261:112–20.

33. Cappellano G, Comi C, Chiocchetti A, Dianzani U. Exploiting PLGA-based biocompatible nanoparticles for next-generation tolerogenic vaccines against autoimmune disease. Int J Mol Sci. 2019;20:204.

34. Bharali DJ, Pradhan V, Elkin G, Qi W, Hutson A, Mousa SA, et al. Novel nanoparticles for the delivery of recombinant hepatitis B vaccine. Nanomed Nanotechnol Biol Med. 2008;4:311–7.

35. Nazeri S, Najafabadi SP, Aali E, Karimpour A, Sarmadi M, Hasanvand M, et al. Comparative study on global genetic diversity and population genetic analysis of orf virus isolates from outbreaks and it's implications for the vaccine development. Am J Biomed Sci Res. 2020;8:235-45.

36. Sarac F, Control PV, Hasoksuz M, Uzar S, Control PV. The use of rabbits in studies of immunity and safety of Contagious Ecthyma (CE) vaccine. Front Vet Sci. 2020;31:75–81.

37. Nagata S. Apoptosis and clearance of apoptotic cells. Annu Rev Immunol. 2018;36:489–517.

38. Liu TY, Hussein WM, Toth I, Skwarczynski M. Advances in peptide-based human papillomavirus therapeutic vaccines. Curr Top Med Chem. 2012;12:1581–92.

39. Landry S, Heilman C. Future directions in vaccines: The payoffs of basic research. Health Aff. 2005;24:758–69.

40. Flower DR. Bioinformatics for Vaccinology. USA: JohnWiley & Sons: Hoboken; 2008.

41. Jorge S, Dellagostin OA. The development of veterinary vaccines: A review of traditional methods and modern biotechnology approaches. Biotechnol Res Innov. 2017;1:6–13.

42. Bull JJ, Smithson MW, Nuismer SL. Transmissible viral vaccines. Trends Microbiol. 2018;26:6–15.

43. Struzik J, Szulc-Dabrowska L. NF-kB as an important factor in optimizing poxvirus-based vaccines against viral infections. Pathogens. 2020;9:1001.

Current Perspectives on Health Sciences, 2022;3(2):82-91

44. Bița R, Răpuntean G, Răpuntean S. Treatment efficacy in udder localisation of contagious ecthyma in sheep and goats. Lucr Știint Ser Med Vet. 2010;53:931-6.

45. Brahma J, Saharia J, Sarma M, Boro P. Successful treatment of contagious ecthyma (ORF) in Assam hill goats by using turmeric powder and aloe vera gel preparation. J Entomol Zool Stud. 2020;8:1454-6.

46. Onyango J, Mata F, McCormick W, Chapman S. Prevalence risk factors and vaccination efficacy of contagious ovine ecthyma (orf) in England. Vet Rec. 2014;175:326.

47. Chauhan SL, Agnihotri D, Batra K, Sharma M, Kumar T, Sindhu N, et al. Detection and therapeutic management of contagious ecthyma (ORF) in a kid. Pharma Innovation. 2021;10:486-8.

48. Dar KH, Tufani NA, Dar SH, Hafiz A, Naikoo MD. Comparative therapeutic management of contagious ecthyma in small ruminants. Intas Polivet. 2015;16:431-5.

49. Lacasta D, Reina R, de Arcaute MR, Ferrer LM, Benito AA, Tejedor MT, et al. Effect of a topical formulation on infective viral load in lambs naturally infected with orf virus. VMRR. 2021;12:149-58.

50. De Clercq E. Cidofovir in the therapy and shortterm prophylaxis of poxvirus infections. Trends Pharmacol Sci. 2002;23:456-8.

51. Geerinck K, Lukito G, Snorek R. A case of human orf in an immunocompromised patient treated succesfully with cidofavir cream. J Med Virol. 2001;64:543-9.

52. Gurel MS, Ozardali I, Bitiren M, San I, Zeren H. Giant orf on the nose. Eur J Dermatol. 2002;12:183-5.

53. Sonvico F, Colombo G, Gallina L. Therapeutic paint of cidofovir/sucralfate gel combination topically administered by spraying for treatment of orf virus infections. AAPS J. 2009;11:242–9.

54. Geerlings E. Sheep husbandry and ethoveterinary knowledge of Raika sheep pastoralis in Rajastan, India. [MSc. Thesis]. The Netherlands: Wageningen University; 2001. SearchEngineWatch Web http://www.pastoralpeoples.org/wp-content/ uploads/2020/01/egfull.pdf Accessed April 19, 2022. 56. Papilend[®],™ Krem Prospektüsü. Hass Tarım&Hayvancılık. SearchEngineWatch Web https://hasstarim.com/hayvancilik-urunleri/hayvanbakim-urunleri/prd-papilend-sigil-kremi-10g Accessed Arpil 19, 2022.

57. Liu JZ, Heo I, Hong MS, Seo JM, Jo SN, Lee JY, et al. The therapeutic effect of ozone on contagious ecthyma in Korean native goats. J Vet Clin. 2006;23:14-7.

58. Sunitha T, Roshin MR, Venkatachalapathy RT. Treatment of contagious ecthyma (ORF) lesions in Malabari goats using ethno veterinary medicine. The Pharma Innovation. 2019;8:927-8.

59. Wang R, Wang Y, Liu F, Luo S. Orf virus: A promising new therapeutic agent. Rev Med Virol. 2019;29:e2013.

60. Adeyeye OA, Osuntade EO, Irekhore OT, Akande FA. Ethnoveterinary practices among small-holder goat farmers in Ogun State, Nigeria. MSP 2021;5:1.