Bovine virus diarrhoea-mucosal disease: prevalence, epizootiology and control measures in the USSR

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Summary: Bovine virus diarrhoea-mucosal disease was described for the first time in the USSR in 1967. The disease occurs in 20 to 80% of farms, depending on geographic and climatic zones of the country. Control measures against the disease include quarantine restrictions and prevention by means of specific preparations of active and passive effect. Passive prophylaxis is conducted by aerosol methods for groups and individuals.


INTRODUCTION

Some researchers (2, 4) consider bovine virus diarrhoea-mucosal disease (BVD-MD) as one of the most important veterinary infections requiring control. They rank this disease in third position after rinderpest and foot and mouth disease. BVD-MD continues to be a problem, largely due to the peculiarities of the disease pathogenesis. The diarrhoea virus affects immunocompetent cells of a susceptible animal and induces a state of immunosuppression. This leads to the activation of facultative pathogenic microflora and creates a favourable background in which the infection may develop. In addition, the complicating factors of BVD-MD virus are: the persistence of the causative agent in the body, the latent course of the disease in most adult animals, the possibility of transplacental transmission and the teratogenic action of virus on the fetus. In our opinion, these are the key features of the diarrhoea virus and are the main cause of economic losses to cattle husbandry and breeding.

PREVALENCE AND EPIZOOTIOLOGY

In the USSR, BVD-MD was first described by Buchnev et al. in 1967 (3). In 1971 Makarevich and Nazarov (10) and Zudilina and Kryukov (17) recorded the disease in a number of farms in the USSR and studied some of its characteristics. In 1976

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ZHIDKOV ET AL. (16) showed that, with the development of industrial husbandry, BVD-MD was more frequently recorded in large industrial units with combined herds of young animals. In most cases there were outbreaks of acute disease caused by cytopathogenic strains of virus diarrhoea virus. In diseased animals which had a leukopenia, general depression and high fever, workers observed the development of ulcerous lesions of nasal glands, wings of nostrils, mucosa of the oral cavity and the gastro-intestinal tract. This was followed by the development of rhinitis and diarrhoea. It must be noted that in most cases, the respiratory form of the disease predominated over the intestinal form. In subsequent years, serological testing of herds without clinical signs but with low performance (lowered milk yields, reproduction disturbances, growth retardation, etc.) revealed the presence of neutralising antibody to BVD-MD virus in serum samples. The possibility was suggested that non-pathogenic strains of virus diarrhoea virus, with a latent course of disease, were circulating on such farms. This hypothesis was later confirmed by immunofluorescence testing and other techniques.

Under experimental conditions using cytopathogenic strains, BVD-MD was reproduced irregularly and the clinical signs (as mentioned above) observed during outbreaks were less pronounced, but the development of a leukopenia, sometimes with a decreased leukocyte count of 1,000 to 1,500 cells/mm³, was consistently observed in infected calves. In diagnostic studies, therefore, this feature of the causative agent is always taken into account. It is not considered the main feature but does provide orientation for further measures.

The form and course of the disease determine the choice of diagnostic methods and these include virological and serological techniques. During outbreaks of respiratory disease in young animals, virological studies have shown that isolation of the diarrhoea virus is rather difficult because of its lability in pathological material. However, a number of isolates were obtained in the USSR and typed as strains of BVD-MD virus (5, 10, 17). Retrospective serological diagnosis, using paired serum samples, has provided an opportunity to confirm the association of diarrhoea virus in more than 30% of outbreaks. In more than 80% of cases, serology has given an indication of the causative agent which circulated in these farms, although its aetiological role in the pathology could not be proved.

It is necessary to differentiate virus diarrhoea from diseases with similar clinical signs: for example, those due to parainfluenza 3 virus, adenovirus, parvovirus, rotavirus, coronavirus, malignant catarrhal fever virus, aphthovirus and vesicular stomatitis virus infections; or to chlamydiosis, colibacillosis, salmonellosis, paratuberculosis, dysentery, helminthic invasion and diseases associated with food intoxications and with copper and molybdenum deficiencies.

In studies on the distribution of the BVD-MD agent, by examination of single samples of serum collected from young and adult cattle, it has been established that this virus circulates in 20 to 80% of the farms examined, depending on the geographic and climatic zones. The virus was more widespread in the zones with intensive husbandry where the improvement of herds is assisted by the purchase of large lots of breeding cattle from other regions of the country as well as from some European and American countries. On farms where antibody to the diarrhoea virus has been detected, the rate of positive animals varied from 15 to 100%. These data show, once more, that virus diarrhoea has a latent course in most cattle.

Aggravation of the disease and the appearance of mass outbreaks are observed more often in animals aged between 2 and 12 months. The disease also occurs in
mixed herds, in large bull-fattening and calf-rearing units and during all seasons
of the year, especially spring and autumn. In such cases, the clinical picture
is variable and depends on the age of the animal and characteristics of the
BVD-MD virus strain. The respiratory form occurs more often in calves of 2
to 4 months of age, whereas in older offspring the course of the disease may
be a remittent diarrhoea. This form of the disease causes fewer deaths but
greater economic losses and is associated with reduced weight gains and retardation
of growth.

On a number of farms, pre-natal and post-natal infections of calves have been
detected with all the ensuing consequences. Pre-natal infection is manifested by
sporadic cases in permanently infected farms. However, when the virus is introduced
into farms which were previously free, pre-natal infection is followed by abortion
and birth of undersized offspring in 20 to 30% of cases.

The above data indicate that subclinical, persistent and chronic forms of the
disease frequently occur in the USSR but they cannot always be diagnosed with
certainty.

**CONTROL MEASURES AND PREVENTION**

Measures for control and prevention are conducted in both disease-free and
infected farms. An infected farm is one where circulation of the agent has been
determined by the presence of antibody even if there are no pronounced clinical signs
and the virus has not been isolated. The measures which are necessary in free
farms must be directed to preventing the introduction of virus. In infected farms
they are directed to preventing aggravation of the disease and treating diseased
animals.

**NON-SPECIFIC MEASURES**

Quarantine restrictions are applied to infected farms, thus ensuring a break in
the epizootic chain between the source of infection and susceptible non-immune cattle.
This means there are restrictions on: introduction and removal of cattle; movement
of animals within farms; feed and dung removal; regrouping of animals and visits
to farms by persons not engaged in handling animals. It is recommended that the
general sanitary regime be strengthened on affected farms and that disinfection be
conducted to prevent agent transmission. Measures are also carried out to increase
the non-specific resistance of the cattle population (e.g. balanced feed and vitamin
enrichment) and to ensure improved cattle management (e.g. summer grazing). It
is recommended that anti-stress and general tonic preparations which improve and
stabilise metabolism (protein hydrolysates of different origins) and immune system
mediators be administered. Special attention is given to protection from transplacental
infection in order to exclude critical consequences for the fetus and the birth of
immunotolerant and apparently healthy calves which are carriers of virus and liable,
in some conditions, to infect the healthy cattle population. This is why virological
control of sperm banks and serological examination of sires is carried out at breeding
and artificial insemination stations.
SPECIFIC MEASURES

Active prophylaxis against BVD-MD is performed by means of a live vaccine prepared from an attenuated local virus strain, VK-1 V1 No. 28, and is only applied on cattle-fattening farms. A dose of $2 \times 10^4 \text{ TCD}_{50}/\text{ml}$ is administered twice in the region of a prescapular lymph node. Twenty-eight to thirty days after vaccination, animals develop neutralising antibodies (titre 1:16 to 1:256) to the virus which ensure full protection against challenge with the homologous epizootic strain of bovine diarrhoea virus. The use of this vaccine involves an economic ratio of seven roubles in profit per rouble of cost.

An inactivated vaccine is more innocuous and that is why it can be used on all types of farms and without any limitations. The local cell culture vaccine against virus diarrhoea is inactivated with ethyleneimine oligomers and is applied twice in volumes of 5 ml and at intervals of 15 to 28 days. The vaccine confers immunity by the 14th day and this becomes fully effective 28 to 30 days after the second vaccination. During this period, the titres of neutralising antibody to virus vary from 1:64 to 1:256. Protection against the disease is ensured for 6 to 8 months.

The vaccine can provide protection against transplacental infection and, when applied 30 to 60 days before calving is expected, contributes to a high concentration of antibodies in the maternal colostrum. Calves born to vaccinated cows and given sufficient colostrum on the third day after birth have high levels of colostral antibodies (more than 1:64) in blood, which confers protection against infection for a period of one and a half months (12). Residual amounts of colostral antibody in animals older than two months do not reduce the effectiveness of vaccination with inactivated vaccine and calves develop an active immunity.

Thus, on affected (antibody-positive) breeding farms, the application of inactivated vaccine against virus diarrhoea is possible in clinically healthy animals in a closed cycle. This includes vaccination of pregnant cows, their offspring at 2 and 8 months of age and heifers on the day of insemination and 1 to 2 months before calving. The scheme aims to prevent the recrudescence of BVD-MD, to decrease the immunosuppressive action of the agent and to improve the indices of herd reproduction. The use of an experimental batch of the vaccine provided an economic ratio of about 40 roubles per animal per year (11).

In some cases, when acute outbreaks of virus diarrhoea occurred, a live vaccine against hog cholera virus, strain K, was used on threatened farms (7, 15). However, the positive effect of this vaccine under experimental conditions, during outbreaks, was found to be of short duration since repeated vaccination of animals did not produce the desired results.

In the USSR, great attention is given to passive prophylaxis and treatment of BVD-MD with serum preparations (1, 6, 14). For the purpose of prophylaxis, these preparations are commonly used in aerosol-dropping (individual treatment) and aerosol (group treatment) techniques. The application by aerosol-dropping on animal mucosa is carried out with a dose of 2 ml into each nasal passage. The procedure is performed on the calves just after birth in the maternity stalls. The aerosol application is carried out in a hermetic chamber with an apparatus that generates particles 5 to 7 microns in diameter under a pressure of 6 atmospheres and at a dose of 10 ml per m$^3$ of chamber. Calves from farm suppliers are treated in groups of 10 to 15 and are kept in the aerosol chamber for 20 to 30 min. The aerosol is applied
just before the calves are introduced into fattening units and these procedures are
repeated, if necessary, every 10 to 15 days until the calves are two months of age.
Convalescent serum is obtained from calves that have recovered and is used on the
same farm or section of the unit. Hyperimmune serum is obtained from calves of
4 to 8 months of age and prepared against the epizootic strain of diarrhoea virus
(VK-1 No. 36), or the inactivated vaccine, according to the method of Tsvetkov et al.
(13).

Immunoglobulins are prepared from calf hyperimmune serum by precipitation
with ammonium sulphate. For the sake of convenience, during transportation and
storage, they are freeze-dried in 200 ml volumes in 0.5 l flasks and are restored to
the initial volume with sterile distilled water just before use. Hyperimmune serum
preparations against BVD-MD virus have often been used in association with similar
preparations against infectious bovine rhinotracheitis virus, parainfluenza 3 virus and
parvovirus infections of cattle. The activity of neutralising antibodies, in preparations
associated with each of the above-mentioned agents and based on the protective index,
is in the range of 3.15 to 5.5 TCD50/ml.

A decrease of 1.5 to 2-fold in the morbidity and mortality rates was obtained as
a result of the aerosol-dropping and aerosol application of serum preparations against
BVD-MD and other concomitant viruses. When compared with a control group, an
additional weight gain of 2 to 6 kg per animal was obtained in fattening units over
a period of 115 to 120 days of feeding (14).

DISCUSSION

It is well known that live vaccines against BVD-MD virus should be employed
with caution because of their possible reactogenicity and ability to aggravate the course
of persistent infection. That is why our locally-produced vaccine against BVD-MD
virus is currently employed on cattle-fattening farms alone. On farms at risk, where
the herd is composed of young sero-negative animals, the use of an inactivated vaccine
is not recommended because its antigenicity is somewhat lower for calves of 7 to 10
days of age and the appearance of strong immunity is delayed until 28 to 30 days
after revaccination. Such calves may become infected before immunity is acquired.
The use of a cyclic scheme of vaccination with inactivated vaccine is only justified
economically in breeding farms of the closed type. In this connection, it may be
necessary to use a combination of the two preparations, depending on the epizootic
situation.

Earlier studies on acute infection with infectious bovine rhinotracheitis virus had
shown that calves withstood challenge for sixteen days after an aerosol application
of hyperimmune serum. This indicated that humoral neutralising antibodies to the
virus are fixed on the mucosa of the calf respiratory tract and provide local protection
against infection. Techniques of aerosol-dropping and aerosol application for bovine
virus diarrhoea and other infections are indeed necessary because of a number of
contra-indications to subcutaneous and intramuscular injection. The most important
of these are: the ability to induce allergic reactions; contamination with heat-resistant
infectious agents; and increased virulence of the agent which circulates on farms with
successive generations of animals, the passive immunity of which is fading. There
is also the possibility of the appearance of virus recombinants. In addition, the cost of large doses of serum necessary for the induction of passive immunity by subcutaneous and intramuscular application should be considered.

In conclusion, not all of the problems associated with bovine virus diarrhoea-mucosal disease have been solved and that is why the exchange of information and international cooperation, at all levels, is not only useful but necessary.

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**DIARRHÉE VIRALE BOVINE-MALADIE DES MUQUEUSES : PRÉVALENCE, ÉPIZOOTIOLOGIE ET MESURES DE PROPHYLAXIE EN URSS. - S.A. Zhidkov et Y.A. Khalenev.**

Résumé : La diarrhée virale bovine-maladie des muqueuses a été décrite pour la première fois en URSS en 1967. La maladie est présente dans une proportion variable (20 à 80 %) des élevages, suivant les différentes zones géographiques et climatiques du pays. Les méthodes de prophylaxie de la maladie comportent la mise en interdit des élevages infectés et des mesures préventives utilisant des produits spécifiques à effet actif ou passif. La prophylaxie passive utilise les techniques d’aérosol appliquées aux groupes d’animaux et aux animaux individuels.


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**DIARRÉA VIRAL BOVINA-ENFERMEDAD MUCOSA: PREVALENCIA, EPIZOOTIOLOGÍA Y MEDIDAS DE PROFILAXIS EN LA URSS. - S.A. Zhidkov y Y.A. Khalenev.**

Resumen: La diarrea viral bovina-enfermedad mucosa fue descrita por primera vez en la URSS en 1967. La presencia de la enfermedad en los ganados varía (de 20% a 80%) según las diferentes zonas geográficas y climáticas del país. Los métodos de profilaxis incluyen la cuarentena de los rebaños infectados y el uso preventivo de productos específicos de efecto activo o pasivo. La profilaxis pasiva consiste en el uso de técnicas de aerosol aplicadas a grupos o animales aislados.

PALABRAS CLAVE: Diarrea viral bovina-enfermedad mucosa - Epizootiología - Inmunoglobulinas - Prevalencia - Prevención - Profilaxis - Técnicas de aerosol - URSS - Vacunas - Virus de la diarrea viral bovina.

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REFERENCES


