DISCONTOOLS

Bovine Herpes Virus 1
Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on Bovine Herpes Virus 1 (BoHV-1). They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control instruments and finally determined the research necessary to develop new or improved tools and measures. Full details are available on the website at http://www.discontools.eu/.

Disease profile

2. Infectious bovine rhinotracheitis / infectious pustular vulvovaginitis (IBR/IPV), is an infectious disease of cattle caused by bovine herpesvirus type 1 (BoHV-1). The virus can infect mainly the upper respiratory tract or the reproductive tract. The virus has a double-stranded DNA genome of about 140 kb which encodes for about 70 proteins, of which 33 structural and up to 15 non-structural proteins have been demonstrated. The viral glycoproteins, which are located in the envelope on the surface of the virion, play an important role in pathogenesis and immunity. Several ruminant alpha-herpesviruses are closely related, both genetically and antigenically, to BoHV-1. These include bovine herpesvirus type 5 (BoHV-5), caprine herpesvirus 1 (CpHV-1), reindeer herpesvirus (CvHV-2), red deer herpesvirus (CvHV-1), buffalo herpesvirus (BuHV-1) and elk herpesvirus (ElkHV-1).

3. The virus is endemic and worldwide distributed in the cattle population although it is not present in several European countries that have successful eradication programmes as specified under the EU Animal Health Law (EU 2020/689). The natural host of BoHV-1 is the bovine with no proof of another relevant domestic or wild ruminant reservoir, although BoHV-1 can establish latency in other species like goat and sheep. There are numerous species of ruminants that can be seropositive to BoHV-1 although it remains unclear if this seropositivity is due to BoHV-1 or infection with another related alpha-herpesvirus.

4. IBR is usually a herd infection with most animals in the group involved. Since only the upper respiratory tract is affected, a dry, non-productive hacky cough is noted. BoHV-1 respiratory outbreaks can be associated with abortion in primary infected cows. Neonatal calves develop a systemic disease with respiratory distress. Often there are subclinical infections, possibly related to husbandry and host conditions or strain differences. Mortality is low but the economic loss can be important due to subclinical infections, secondary bacterial infections and especially trade implications.

Risk

5. There is no reported incidence in humans. Infection is mainly transmitted by direct animal contact, trade and more rarely by indirect contacts (e.g. via persons or instruments). Due to the limited environmental stability, the virus remains for some days infectious on clothing, bedding, feed, and technical devices. Following infection, the virus stays lifelong latent in the affected neuronal ganglia and may be reactivated upon stress stimuli. Vaccination protects efficiently from clinical disease but not reliably from induction of a carrier status with possible virus reactivation and shedding. In cattle, seronegative latent BoHV-1 carriers (SNLC) have been demonstrated experimentally but their importance in the field remains unclear. In particular, more epidemiological data on the SNLC reactivation rate in BoHV-1 free regions needs to be collected and studied. It is also important to evaluate the risk of recurrence of BoHV-1-infections once vaccination has been stopped. This is also of high importance in BoHV-1 free units, such as bull studs.

Diagnostics

6. Both conventional and real time PCRs can be used to detect the virus. Retrospective diagnosis of BoHV-1 infection can be done by measuring antibody titres in paired sera samples. Antibody detection is via serum-neutralisation (SN) tests and various BoHV-1 indirect and blocking ELISAs which are currently available. However, neutralisation tests are no longer the gold standard as a range of other methods now exist including the gB-ELISAs which are generally more sensitive and also highly specific. The use of marker vaccines is important in the differentiation of infected and vaccinated animals that can

be made by the simultaneous use of conventional BoHV-1 ELISAs detecting whole virus or glycoprotein B (gB) antibodies and marker ELISAs detecting glycoprotein E (gE) antibodies.

7. A confirmatory test for the presence of gE-specific antibodies using different protocols does not exist. Consequently, the development of an independent and sensitive confirmatory test would be important for establishing the status of animals giving borderline responses in the gE ELISA. This would also be of great advantage in eradication programmes using gE-based DIVA vaccines. A gE assay with an improved sensitivity for bulk milk samples would facilitate marker vaccine control/eradication in dairy herds. Additional tests should be developed, allowing the detection of BoHV-1-specific antibodies with a high sensitivity and specificity, which are different from the gB-ELISAs (e.g. gC-ELISA or gG-ELISA or gD-ELISA). Such assays could allow the classification of unspecific or cross-reactions in the conventional BoHV-1 ELISAs.

Vaccines.

8. Live-attenuated and inactivated vaccines are commercially available which can be administered intramuscularly or intranasally. Various sub-unit and vectored vaccines have also been tested experimentally. Live-attenuated vaccines are administered either in one injection or two at a 3 weeks interval in a primary course. Inactivated vaccines require two administrations, three weeks apart, in a primary course with booster vaccinations every 6 months thereafter. The efficacy of BoHV-1-vaccines is especially focussed on the reduction of clinical signs and on the repression of wild type BoHV-1.

9. Marker vaccines are commercially available and are licensed by a number of companies with DIVA capacity which is based on the absence of gE in inactivated vaccines or the gE gene delete virus in live-attenuated vaccines. Marker vaccines might be further improved with a higher efficacy, i.e. inducing long term protection (> 1 year). After intramuscular administration marker vaccines will not become latent, which is a significant improvement to currently available conventional vaccines. Other improvements would include the development of adjuvanted live attenuated vaccines for long lasting immunity, prolonged delivery devices and possibly RNA vaccines.

Pharmaceuticals

10. As with other viral diseases, there is no direct treatment for the infection and antivirals are not needed for the effective control of BoHV-1. There might be an interest to use antivirals (anti-herpesvirus compounds) to face BoHV-1 outbreaks in free herds and countries, where vaccine is no longer used and not available. However, at current both the costs of development and production are too high and their use is not allowed in the EU.

Knowledge

11. Research should be focussed on immunological aspects of the interaction of BoHV-1 with the host immune system: e.g. on viral genes downregulating the host immune system; immuno-modulation (adjuvants, cytokines etc.), vaccine application, and factors involved in latency. The contribution of other ruminants to the epidemiology of viruses related to BoHV-1 is small but should not be discounted in unexplained outbreaks in cattle, particularly relating to goats, sheep, water buffalo, and wild ruminants. Other requirements include the development of molecular arrays to identify and compare BoHV-1 sub-types and related virus and full-length sequences of selected subtypes/strains to characterize further strains.

Conclusions

12. BoHV-1 infections are still of major economic impact in the cattle industry. This not only as an infection of cattle standing on its own, but also as part of the Bovine Respiratory Disease complex, in which several viruses and bacteria are involved. Currently eradication programmes for BoHV-1 are running in several European countries, where gE-negative DIVA vaccines are used in combination with the companion diagnostic gE-ELISA tests. The currently used DIVA vaccines and the accompanying diagnostic tests have been the basis of successful eradication programmes. In addition, the most important factors in any BoHV-1 eradication programme are biosecurity measures like separation, marking and fast slaughtering of BoHV-1 positive cattle. Despite this, both the available vaccines and diagnostics can/need to be further improved for more efficient control.