Preliminary Classification of the Bovine Respiratory Complex into Different Levels of Severity

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Abstract

Despite prophylactic measures, mainly including vaccination programs and management measures, respiratory disease remains the major cause of economic losses in the bovine species. Choice of treatment is currently mainly based on the clinicians' personal experience.

A theoretical method has been proposed earlier to classify this syndrome into four grades of severity : Grade 1, subclinical disease (no treatment); Grade 2, compensated clinical disease (antibiotics only); Grade 3, noncompensated clinical disease (antibiotics + antiinflammatory drugs); and Grade 4, irreversible clinical disease (no treatment).

In order to realize this theoretical classification under field conditions, three techniques, each one evaluating the oxygen transport chain at a different level, have been studied and validated, i.e. pulse oximetry, lactate dosage and the lobeline test. Afterwards, measurements were performed on calves suffering from acute respiratory disease and a preliminary classification was established. This novel approach could orientate and economize therapeutic strategies in bovine respiratory disease.

Introduction

Despite prophylactic measures, mainly including vaccination programs and management measures, respiratory disease remains the major cause of economic losses in bovine species. Most calves do need a treatment for respiratory disease during somatic growth. Mortality, diminished zootechnical performances caused by irreversible pulmonary lesions and high costprice of therapeutic interventions explain the enormous economical impact of respiratory diseases. Bovine practitioners dispose of numerous pharmacological substances to treat these pathologies. Those substances can be divided into three major categories: antimicrobial agents, modulators of inflammatory reaction and substances correcting mechanical disorders. Scientific literature is very well documented in description of the action of numerous pharmacological substances utilised in standardised conditions. On the other hand, this literature is nearly non-existent concerning the application of therapeutic strategies in function of severity level of different bovine respiratory syndromes. Actually, neither clinical measures nor measures of complementary examinations exist to consider control of these problems in a global way, not only in function of maximal efficacity but also in function of minimal residus and treatment costs. Different techniques have been validated to evaluate precisely the functional impact of respiratory pathologies in practice. Description of these techniques is subject of the first part in this text. In the second part, a preliminary classification is made of the four grades of severity of respiratory disease, namely subclinical disease (Grade 1), compensated clinical disease (Grade 2), non-compensated clinical disease (Grade 3) and irreversible clinical disease (Grade 4) (1).

Description of Used Techniques

1. Measurement of ventilatory reserve (lobeline test)

Spirometry is used extensively in human medicine to measure the maximal ventilatory parameters (MVP) of patients (2). Measurement of spirometric parameters allows the characterisation of respiratory lesions, improving diagnostic and therapeutic strategies. Since spirometry requires patient cooperation, it has been unavailable in veterinary medicine. Yet, MVP measurement could replace the complicated pulmonary function tests (3) currently used for research and clinical purposes in calves. In a recent study devoted to calves, we showed that the non-cooperation obstacle could be overcome by intravenous injection of lobeline, a respiratory analeptic (4). According to this, we demonstrated that most calves' MVP could be reliably assessed during the period of maximal ventilatory changes induced by lobeline administration. Afterwards, normal values of

Adapted from the Proceedings of the XX World Association for Buiatrics Congress, Sydney, Australia, July, 1998.

MVP and effects of somatic growth on these parameters were defined as equations of prediction relating MVP to biometric variables in healthy Friesian calves and Belgian White and Blue calves (5). These normal values are required for the determination of pathologic MVP changes induced by calf specific respiratory diseases and for subsequent interpretation of individual MVP values.

2. Pulse oximetry

Measurement of arterial hemoglobin oxygen saturation is an important means to evaluate effectiveness of the oxygen transport chain. Assessment is usually performed based on an arterial blood sample analysed by a blood gas analyzer. Pulse oximetry is a non-invasive method of measuring percentage oxygen saturation of arterial hemoglobin, based on differential absorption of red and infrared light and widely used in human anesthesia and ICU. However, in veterinary medicine applications are rather limited (6, 7). Practicality and accuracy of a portable pulse oximeter and the accompanying nasal septum probe (VetOx 4402, SDI, Waukesha, USA) was assessed in 46 healthy and 6 diseased bovines, suffering from acute respiratory distress syndrome (8). In healthy bovines three different probe sites, i.e. the tail, the nasal septum and the genital mucosae, provided a continuous, stable, intense and regular signal. There was no significant difference between the two methods when the probe fitted to the animals' tail. Shaving, pigmentation and movement artefacts were its most important inconvenients. Difference was statistically significant when the probe was attached to the nasal septum ($\Delta < 2.93$ %) or to the genital mucosa (only females) ($\Delta < 2.2$ %). Partial obstruction of the upper airways, head movements and limited mucosal surface in younger heifers respectively appeared to be their major disadvantages. Measurements performed on severely diseased animals (probe placed on the tail) with low values of hemoglobin oxygen saturation showed no significant differences with the reference method and were highly correlated ($r = 0.99$). Therefore, pulse oximetry could provide to the clinicians an accurate, immediate, non invasive and cheap method to assess the arterial hemoglobin oxygen saturation in cattle and to evaluate severity of failure of the oxygen transport chain in case of acute respiratory distress syndrome.

3. Blood lactate dosage

Blood lactate measurement is a universally used parameter to assess muscular aerobic capacity and physical condition in horses as in man (9, 10). It also revealed to be a reliable prognostic measure in case of colic in the horse (11, 12, 13).

Respiratory disease challenges oxygen transport chain in two ways : a diminished oxygen transfer from the lungs to the arterial blood and an elevated oxygen consumption by an increased work of breathing. The relative contribution of anaerobic pathway to metabolism becomes more important and consequently blood lactate could increase. Since portable blood lactate analysers are currently available and widely used in human and equine sports medicine (14), it seemed to be interesting to study the reliability of portable analysers in calves in the aim of assessing afterwards the interest of blood lactate concentrations in the prognosis of bovine pulmonary disorders. A comparison was made between a reference laboratory method and a portable blood lactate analyser (Accusport). Accusport is a small, cheap apparatus measuring instantaneously blood lactate concentration in a single droplet of blood based on a biochemical reaction and reflexphotometry. Results of both techniques were statistically different but correlation was very high (15). Therefore it may be concluded that blood lactate measurement in calves may be performed with portable analysers and may be used in the field by bovine practitioners.

Materials and Methods

During the winter of 96-97, thirty double-muscled calves (12 males/18 females, weighing between 65 and 350 kg, between 3 weeks and one year old) were referred to the animal hospital at the faculty of veterinary medicine, Liège. All calves were suffering from bronchopneumonia (variable etiologies). One hour after arrival calves were submitted to a clinical examination and a battery of supplementary examinations, namely blood gas analysis, pulse oximetry, lobeline test and blood lactate dosage. Clinical examination was repeated daily, other measurements were repeated at return to clinical health or when no response was seen after treatment. Treatment of diseased calves was standardized in the following way:

- none in case of minor clinical signs
- antibiotics (florfenicol) in case of moderate clinical signs
- antibiotics (florfenicol) and antiinflammatory drugs (flunixine meglumine or prednisolone sodium succinate) and eventually bronchodilators (clenbuterol[a] + ipratropiumbromide) in severe cases.

Results

A preliminary classification of the 4 grades of severity was established and is presented in Table 1.

[a] *Editor's note: The use of clenbuterol in food animals in the United States has been declared illegal by the Food and Drug Administration (FDA).*

Table 1. Preliminary classification into different levels of severity.

	SatO2 (%)	PLC (mmol/L)	VR
Grade 1	> 95 %	< 2	↓
Grade 2	> 95 %	< 2	↓↓
Grade 3	> 85 %	< 4	none
Grade 4	< 85 %	> 4	none

SatO2 : Arterial hemoglobin oxygen saturation ; PLC : Plama lactate concentration ; VR : Ventilatory reserve.

Discussion

The lobeline test, which evaluates the oxygen transport chain at the level of the lung, revealed to be very sensitive and very interesting in cases of minor respiratory problems where pulse oximetry and lactate dosage couldn't detect any changes. Maximal minute ventilation was significantly diminished in subclinically ill animals. Grade 2 animals had a highly diminished maximal ventilation and a significantly elevated basic ventilation. Grade 3 and 4 showed no ventilatory reserve. Pulse oximetry could measure alterations of arterial hemoglobin saturation in grade 3 and 4 animals and a saturation < 85% was indicative for an irreversible evolution. Blood lactate dosage proved to be extremely easy and interesting to separate surviving animals from non-surviving animals. Survivors never had blood lactate concentrations above 4 mmol/L. Non-survivors always showed increased lactate concentrations above 4 mmol/L during the last twenty-four hours of their life. Therefore it may be concluded that this measurement could be a very helpful instrument to increase accuracy of prognosis.

Conclusions

These preliminary results show that the theoretical classification of bovine respiratory disease into different levels of severity can be realised in practice. Further measures should be done on a large number of animals to establish precise criteria for every severity level and to make correlations with clinical parameters.

Acknowledgements

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CVM Update

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In Fiscal Year (FY) 1998, FDA funded seven (7) cooperative agreements under the President's Food Safety Initiative. These projects may be funded for up to two or three years depending on progress and the availability of these research funds to study the microbiological hazards associated with the food animal production environment which includes animal feeds.

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On-farm risk factors for zoonotic enteropathogens associated with cattle feed and water	Dale Hancock	Washington State University Pullman, WA	$152,735
Waterborne dissemination of *Escherichia coli* 0157:H7	Charles Kaspar	University of Wisconsin-Madison, WI	$102,853
STEC, *salmonella* virulence and antibiotic resistance in cattle and feed	David Acheson	New England Medical Center Boston, MA	$198,192
Factors affecting numbers of acid-resistant *Escherichia coli* in cattle	James Russell Ithaca, NY	USDA/ARS	$72,530
Survey of antimicrobial resistant *Enterococci* in animals	Marcus Zervos	William Beaumont Hospital Royal Oak, MI	$148,448
Control of EHEC in cattle by probiotic bacteria	Michael Doyle	University of Georgia Athens, GA	$116,026
Evaluation and use of BAM/FDA and rapid methods for on-farm survey	Ann Draughton	University of Tennessee Knoxville, TN	$151,482

Additional information about these agreements is available from Dr. David B. Batson, Center for Veterinary Medicine (HFV-502), Food and Drug Administration, 8401 Muirkirk Rd., Laurel MD 20708, 301-827-8021.

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CVM UPDATE

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October 30, 1998

Minor Species/Minor Use Report Available

In the October 29, 1998, Federal Register, FDA announced the availability of a report entitled, "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Uses." The report contains proposals for changes to the approval process for new animal drugs intended for use in minor species and for minor uses in major species. Minor species are defined in the Code of Federal Regulations as "animals other than cattle, horses, swine, chickens, turkeys, dogs, and cats."

This report is the Agency's response to a requirement of the Animal Drug Availability Act (ADAA) of 1996 that the Secretary of Health and Human Services consider and announce proposals to facilitate approvals for minor use drugs. Implementation of these proposals should increase the number of legally available new animal drugs for use in minor species and for minor uses. Many of the proposals require changes in the Federal Food, Drug, and Cosmetic Act before regulations can be written and the changes implemented.

Copies of this report may be obtained from CVM's Internet Home Page (http://www.fda.gov/cvm) or by calling or writing CVM's Communications Staff at FDA/Center for Veterinary Medicine, HFV-12, 7500 Standish Place, Rockville, MD 20855, 301-594-1755. Send one self-addressed adhesive label to assist in processing your requests.

The Agency is requesting comments on this report at any time. Written comments on the report should be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Comments should be identified with Docket Number 97N-0217. FDA will also accept e-mail comments. They should be labeled as comments, be identified with Docket Number 97N-0217, and be addressed to jbutler@bangate.fda.gov. The Agency will make paper copies of these comments and will place them in the public docket.

Questions about the minor species/minor use section [section 2(f)] of the ADAA may be directed to Dr. George A. (Bert) Mitchell, Center for Veterinary Medicine (HFV-6), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-5587, e-mail: gmitchel@bandate.fda.gov. Further information about the changes proposed in the report to the approval process is available from Dr. Linda Wilmot, Center for Veterinary Medicine (HFV-114), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, (301) 827-7450, e-mail: lwilmot@bangate.fda.gov.

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Abstracts

Diagnostic reliability of clinical signs in cows with suspected bovine spongiform encephalopathy

U. Braun, E. Schicker, B. Hörnlimann
Veterinary Record (1998) 143, 101-105

The clinical findings in 50 cows with suspected and subsequently confirmed bovine spongiform encephalopathy (BSE) (group A) were compared with the clinical signs in 22 cows with suspected BSE, but with no histological evidence of the disease (group B). The chi-square test for association was used to compare the frequencies with which diagnostic signs or combinations of signs, were positive in the cows of groups A and B. When the frequency of a sign differed significantly, its sensitivity, specificity, efficiency and positive and negative predictive values were calculated. With respect to changes in behaviour the cows in group A more frequently showed increased excitability, nervous ear and eye movements, increased salivation and increased licking of the muzzle than the cows of group B. With respect to changes in sensitivity the cows in group A were more frequently hypersensitive to touch, noise and light than the cows of group B. With respect to changes in locomotion the cows in group A were more frequently ataxic than the cows in group B.

Persistence of the activity of topical ivermectin against biting lice (*Bovicola bovis*)

B. Clymer, K.M. Newcomb, W.G. Ryan, M.D. Soll
Veterinary Record (1998) 143, 193-195

To assess the persistence of the activity of topical ivermectin against a natural challenge with biting lice (*Bovicola bovis*), 90 mixed-breed cattle that had been treated to remove lice, were blocked by bodyweight within sex and randomly allocated to three treatments: untreated control, doramectin at 200µg/kg by subcutaneous injection, and ivermectin at 500 µg/kg by topical application. Forty-five pens were blocked into three groups of 15, and the blocks of pens were randomly allocated to three 14-day challenge periods starting 21, 28 and 35 days after treatment. There were five pens per treatment for each challenge period, and one *B bovis*-infested donor calf was introduced into each pen containing two principal calves at the start of the challenge period for that block of pens. The calves were examined thoroughly for *B bovis* seven, 14 and 21 days after the introduction of the donors. There were no significant differences between the control and doramectin groups for the numbers of animals infested, or the geometric mean louse counts at the final examination for any of the challenge periods. At the final examination for each challenge period, the louse counts of the cattle treated with topical ivermectin were all zero, and significantly ($P<0.05$) fewer cattle treated with topical ivermectin were infested than either the controls or cattle treated with doramectin.

Prevalence, incidence and geographical distribution of Johne's disease in cattle in England and the Welsh borders

B. Cetinkaya, H.M. Erdogan, K.L. Morgan
Veterinary Record (1998) 143, 265-269

The prevalence, incidence and geographical distribution of clinical Johne's disease in dairy cattle in England and the border regions of Wales were determined by a postal survey of 3772 dairy farmers. The study area was divided into three regions; south, central and north. The response rate was 78·3 per cent. The proportion of farms that reported 'ever' having the disease was 17·4 per cent. For the 10 years between 1985 and 1994 it was 4·9 per cent, and only 1·5 and 1·3 per cent in 1993 and 1994 respectively. The highest prevalence figures were always in the south. The incidence rate of clinical disease was 3·0/10,000 cow-years in both years in all herds and 16·7 and 22·8/1000 cow-years in infected herds in 1993 and 1994 respectively. An estimate of the criterion validity of diagnosis by farmers was obtained by comparing the reporting of the clinical signs with positive veterinary or veterinary investigation centre diagnoses. the proportion of farmers reporting one or other of the correct clinical signs was 95·3 per cent, and 70·6 per cent reported both correct signs (diarrhoea and weight loss).

Abstracts

Description of 14 cases of bovine hypokalaemia syndrome

N. Sattler, G. Fecteau, C. Girard, Y. Couture
Veterinary Record (1998) 143, 503-507

The records of 14 cases of bovine hypokalaemia observed between 1983 and 1996 were reviewed. The most common history included a protracted, often infectious, disease. All age groups were represented. Although previously reported as a risk factor, isoflupredone acetate had not been administered to five of the cases. The following clinical signs were recorded in 10 cases: abnormal position of the head and neck, severe weakness, rumen hypomotility or atony, abnormal faeces, anorexia and tachycardia. Cardiac dysrhythmia was observed in six cases. Acid-base imbalance (alkalosis in 10 cases), hyperglycaemia and increased activities of aspartate aminotransferase and creatine kinase were associated with hypokalaemia ranging from 1·35 to 2·49 mmol/litre. Treatments included symptomatic treatment, supportive care and potassium chloride given intravenously and orally at an average total daily dose of 42 g/100 kg bodyweight (26 g by mouth and 16 g intravenously) for an average of five days. Eleven cases recovered after an average of three days.

Prognostic indicators for toxic mastitis in dairy cows

M. J. Green, P. J. Cripps, L. E. Green
Veterinary Record (1998) 143, 127-130

During a three-year study, 54 cows with toxic mastitis were examined and a number of clinical and laboratory measurements were taken. Twenty-five (46·3 per cent) of the cows died, and in comparison with those which survived, they had a significantly higher packed cell volume (PCV) ($P<0·01$), longer eyelid skin tent time ($P<0·01$) and lower rectal temperature ($P<0·01$). In a model designed to predict the probability of survival, these variables correctly predicted survival in 84 per cent of cases and death in 73 per cent of cases. The cows with toxic mastitis had a significantly higher PCV than a normal cohort of cows sampled at the end of the study.

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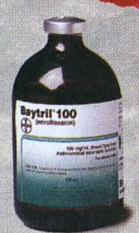

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