Validation of different vaccination protocols against bovine respiratory disease in high-risk calves vaccinated after arrival on Swiss veal farms

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Validierung von unterschiedlichen Impfschemata gegen enzootische Bronchopneumonie für junge Kälber nach Anlieferung auf Schweizer Mastbetrieben

Es war das Ziel dieser Feldstudie, bei Kälbern nach Ankunft auf dem Mastbetrieb die Effektivität verschiedener Impfschemata gegen die enzootische Bronchopneumonie (EBP) zu erfassen. Unter Praxisbedingungen wurden auf vier Schweizer Kälbermastbetrieben jeweils drei Mastdurchgänge ausgewertet. Dabei wurden kommerziell erhältliche Impfstoffe gegen das bovine respiratorische Synzytialvirus (BRSV), das bovine Parainfluenzavirus Typ 3 sowie gegen *Mannheimia haemolytica* eingesetzt. Die Kälber (n = 418) wurden am Tag nach ihrer Ankunft auf den Betrieben entweder mit einem Lebendimpfstoff (LV) oder einem inaktivierten Impfstoff (KV) vakziniert oder sie erhielten ein Placebo (P). Nach 21 Tagen erfolgte eine Booster-Impfung im reduzierten Crossover-Design, sodass sich fünf Impfschemata ergaben: LV/LV (n = 83), LV/KV (n = 82), KV/LV (n = 84), KV/KV (n = 80) und P/P (n = 89). Alle oralen und parenteralen Behandlungen mit Antibiotika sowie die Leistungsdaten (insbesondere die täglichen Zunahmen) wurden erfasst und ausgewertet. Von 223 Kälbern wurden zudem Blutproben entnommen, um im Serum die BRSV-Antikörper sowie die Haptoglobinkonzentration zu bestimmen. Es ergaben sich bei der Auswertung keine signifikanten Unterschiede zwischen den verschiedenen Impfschemata im Hinblick auf die Zahl und Dauer antibiotischer Behandlungen. Auch die Leistungsparameter wurden durch das Impfschema nicht beeinflusst. Es lässt sich schlussfolgern, dass keines der Impfschemata als besonders empfehlenswert angesehen werden kann. Die Impfung der Kälber nach Ankunft auf dem Mastbetrieb erfolgt offen-

Summary

The objective of the study was to evaluate the efficacy of different vaccination protocols against bovine respiratory disease (BRD) for calves newly arrived at veal farms. Four farms in Switzerland were enrolled under field conditions each with three fattening periods. Commercially available vaccines were administered against bovine respiratory syncytial virus (BRSV), bovine parainfluenza virus type 3 and, partly, Mannheimia haemolytica. The calves (n = 418) were vaccinated on the day of arrival on the farms with either a live vaccine (LV), a killed vaccine (KV) or a placebo (P). After 21 days, a booster vaccine was administered in a reduced crossover design resulting in five vaccination protocols: LV/LV (n = 83), LV/KV (n = 82), KV/LV (n = 84), KV/KV (n = 80) and P/P (n = 89). Blood samples were collected from 223 calves on the day of arrival (day 1), day 3, day 21 and day 28 to assess BRSV antibodies and haptoglobin. Oral and parenteral antibiotic treatments were assessed as well as performance data, in particular daily weight gain. The seroprevalence of BRSV at time of arrival was high (86 %). Results revealed neither significant differences in respect to number of antibiotic treatments nor in the performance data for any of the applied vaccinations protocols. It is concluded that, considering the frame conditions, any vaccination of calves on arrival on the veal farm seems to be at an inappropriate point of time, i. e. an effective subsequent protection against BRD cannot be achieved in this way.

Keywords: BRD, BRSV, PI-3, DWG, prevention, treatment, vaccination

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sichtlich zu einem Zeitpunkt, der nicht geeignet ist, um einen effektiven Schutz der Tiere vor enzootischer Bronchopneumonie während der Mastperiode zu ermöglichen.

Schlüsselwörter: EBP, Impfung, Mastkälber, PI-3, Prävention, Therapie, Tageszunahmen

Introduction

Roughly 190 000 veal calves are slaughtered per year in Switzerland.[23] About two-third are raised on small farms in mountainous areas, where milk collection may be difficult.[17] Further 70 000 veal calves are fattened yearly in groups of 30–100 calves on farms on a fee basis by companies using milk replacer or by-products of the dairy industry.[2]

Most male calves are marketed at an age of 3–5 weeks. They are transported by traders to fattener operations which produce either veal calves (120 kg carcass weight within 14–18 weeks) or beef cattle (300 kg carcass weight within 10–12 months).[24]

Predominantly during the first four weeks after purchase by the fattener, bovine respiratory disease (BRD) represents the most important health issue leading to low daily weight gains, high expenses for veterinary treatments and drugs (typically CHF 50–100/calf in the first weeks), and significant mortality (typically 2–4 %).[15,17,18,27] According to data from the national registration system on the use of antibiotics in food-producing animals, 89 % of all antibiotic treatments administered to calves are related to BRD.[5]

To cope with this problem, antimicrobials have been used for decades more or less excessively for metaphylaxis and therapy orally and/or parenterally. In the last years, however, the use of antimicrobials has been criticized due to its limited efficiency[3] and the concomitant risk of an increasing spread of resistant isolates of the most relevant infectious agents (i. e., *Pasteurella multocida, Mannheimia haemolytica, Mycoplasmopsis bovis*)[28,31] with consequences also for human health.[12] Thus, prevention is crucial. Most promising approaches focus on the improvement of the constitution of the calf already on the dairy farm ("preconditioning"),[26] a minimization of transport stress and an optimization of the housing management in the fattener unit, i. e., feeding, hygiene and ventilation.[6,18,27] Unfortunately, these strategies cannot solve the problem of commingling many young calves from a variety of dairy farms in the fattener unit due to the small-scale dairy farms in Switzerland.

Vaccination is considered as a tool to reduce problems caused by BRD in purchased calves. Although worldwide a lot of calves are vaccinated using either inactivated or attenuated vaccines year by year, the effects on morbidity, mortality, proportion of relapses, return on investment (ROI) and protection rate of vaccinated calves vary between the farms tremendously.[8,10,30] Generally acknowledged recommendations in respect to the vaccine (inactivated *vs.* attenuated), route of administration (intranasal *vs.* parenteral), booster interval, time point of administration (directly after arrival *vs.* days/weeks thereafter) do not exist. Moreover, in the last years, the immunomodulatory effect of vaccines in addition to the adaptive immune response is a matter of debate – the relevance of this issue for vaccinations against BRD is, however, simply unknown.[1,4]

Accordingly, it was the aim of this study was to establish an optimal vaccination protocol under Swiss conditions. We hypothesized that no significant differences in morbidity, mortality, growth performance, or antimicrobial use among calves receiving different vaccination protocols after arrival at the veal farm can be demonstrated.

Materials and Methods

Farms

Four veal farms located in Eastern Switzerland were included in the study. The study conducted over a one-year period was approved by the cantonal veterinary office Zurich (approval number TVA ZH066/17).

The farms raised 28–56 calves per fattening period in different housing systems according to Swiss federal law for animal protection (Table 1). All farms had indoor stables with straw bedding. Three farms had an outdoor area in addition. Three fattening periods per farm were evaluated.

Feeding

The calves were fed *ad libitum* using automatic milk feeders without identification of single animals (Foerster TA-KR1 or Foerster TA-P7). A mixture of milk and milk replacer (UFA 201) or solely milk replacer (UFA MAT 105/106) were offered. Hay or roughage cubes (UFA 215 Fibrafit) were available as supplementary feed.

Study design

The field study was conducted between June 2018 and October 2019. Data were collected on day 1, day 3, day 21 and day 28 after the calves arrived at the veal farm delivered by the cattle dealer. Each calf was examined the day after arrival (day 1) to assess the health status based on a standardized examination protocol (Supplement 1). Only clinically healthy calves were included in the trial, calves with fever

Table 1: Characteristics of the four veal farms included in the study; CNf – label Coop Natura-farm®, IPS – label IP Suisse (i.e., Swiss Association of Integrated Producing Farmers), QM – conventional production.

Number of the farm	Production system	Fattening periods per year	Calves per batch	Housing system	Pen space per calf [m²]	Automatic milk feeder	Feeding
# 1	IPS	3	28–30	Indoor and outside pen	4,5	Förster TA-KR1	30 % milk and UFA 201; hay
# 2	QM	3	50–56	Indoor pen	2	Förster TA-P7	UFA MAT105/ MAT 106; UFA 215 Fibrafit
# 3	CNf	3	30	Indoor and outside pen	4,5	Förster TA-P7	UFA MAT105/ MAT 106; hay
# 4	CNf	3	49–50	Indoor and outside pen	4,5	Förster TA-P7	UFA MAT105/ MAT 106; hay

(rectal temperature ≥ 39,8 °C) and/or symptoms of pneumonia, otitis media, diarrhea or omphalitis were treated immediately and excluded from the study.

At arrival, each calf of the group was randomly assigned to one of five vaccination protocols (Table 2). Calves were vaccinated on day 1 and day 21 with either a commercially available approved live vaccine (LV) (Rispoval® RS + PI3; attenuated live vaccine containing *bovine respiratory syncytial (BRS) virus*, thermosensitive strain 375, $10^{5,0}$ – $10^{7,2}$ $GKID_{50}$, *bovine parainfluenza 3 (PI-3) virus*, thermosensitive strain RLB103, $10^{5,0}$ – $10^{8,6}$ $GKID_{50}$) and/or a commercially available approved killed vaccine (KV) (Bovilis® Bovigrip; inactivated *PI-3 virus* ($10^{7,3}$ – $10^{8,3}$ $TCID_{50}$), inactivated *BRS virus* ($10^{5,5}$ – $10^{6,4}$ $TCID_{50}$), inactivated *Mannheimia haemolytica* (9×10^9 cells), aluminium hydroxide, Quil A). Control animals received subcutaneous injections of saline (NaCl Braun 0,9 %; B. Braun Medical® AG).

During the fattening period all animals were under daily supervision of the farmer. General clinical status of the calves was also checked by a veterinarian (DS) on day 1, day 3, day 21 and day 28.

Blood serum was collected from 50 % of the animals per batch by jugular venipuncture utilizing anticoagulant-free tubes (VACUETTE® Serum 9 ml, Greiner Bio-One, Kremsmuenster, Austria) prior to the initial vaccination (day 1), three days after the initial vaccination (day 3), prior to the booster vaccination (day 21) and seven days after the booster vaccination (day 28).

Weight Data

Body weight of each calf was assessed on day 1 and day 28 after arrival using an electronic livestock scale. Daily weight gain (DWG) was calculated based on the weighing of each calf at day 1 respectively day 28 after arrival on the farm, the body weight at the time of slaughter and the fattening duration.

Body weight at time of slaughter was calculated based on carcass weight and carcass yield (%; based on evaluations of UFA AG; Supplement 2).

Treatments

All animals received a prophylactic oral treatment via automatic feeder with amoxicillin (Amoxan 70 ad us. vet., ufamed AG, Sursee, Switzerland; 30 g/100 kg per day) from day 1 for 5–10 days.

During the study period, the veterinary practice of the respective farm was available for any acute treatments. Each

Table 2: Vaccination protocols for calves tested in this study on Swiss veal farms.

Vaccination protocol	Day 1	Day 21
LV/LV	i. n. application of LV [2 ml]	i. n. application of LV [2 ml]
LV/KV	i. n. application of LV [2 ml]	s. c. application of KV [5 ml]
KV/LV	s. c. application of KV [5 ml]	i. n. application of LV [2 ml]
KV/KV	s. c. application of KV [5 ml]	s. c. application of KV [5 ml]
P/P	s. c. application of saline [5 ml]	s. c. application of saline [5 ml]

LV = live vaccine; KV = killed vaccine; P = placebo; i. n. = intranasal; s. c. = subcutaneous.

calf that became clinically ill was recorded and treated according to a standardized treatment protocol (Supplement 3). All treatments were documented.

Respiratory symptoms indicating BRD (frequent coughing and/or respiratory rate > 36 / min and fever ≥ 39,8 °C) were treated using florfenicol (20 mg/kg s. c.; Nuflor® 300 mg/ml, MSD Animal Health GmbH, Lucerne, Switzerland) three times (q 48 hours) and meloxicam (0,5 mg/kg s. c.; Metacam® 20 mg/ml, Boehringer Ingelheim GmbH, Basel, Switzerland) for one to three days. If symptoms of an O*titis media* (headshaking, head-pressing, hanging ear and fever ≥ 39,8 °C) occurred, oxytetracycline (20 mg/kg s. c.; Cyclosol LA, Dechra Veterinary Products Suisse GmbH, Basel, Switzerland) was administered three to four times (q 72 hours) and meloxicam (0,5 mg/kg s. c.; Metacam® 20 mg/ml, Boehringer Ingelheim GmbH, Basel, Switzerland) for one to three days or dexamethasone (0,3 mg/kg s. c.; Dexatat®, Graeub AG, Bern, Switzerland) once. In case of symptoms of diarrhea (watery feces, encrusted perianal region, dehydration), oral electrolyte solution was offered and meloxicam (0,5 mg/kg s. c.; Metacam® 20 mg/ml, Boehringer Ingelheim GmbH, Basel, Switzerland) was administered once. An omphalitis (diagnosed based on a hunched spine, painful umbilical swelling) was treated using amoxicillin (15 mg/kg s. c.; Duphamox® LA, Zoetis Schweiz GmbH, Delémont, Switzerland) for eight days (q 24 hours) and meloxicam (0,5 mg/kg s. c.; Metacam® 20 mg/ml, Boehringer Ingelheim GmbH, Basel, Switzerland) for one to three days.

If more than 20 % of the calves in the pen were clinically ill, an oral group treatment was administered. Either doxycycline (Primadox 50 ad us. vet., ufamed AG, Sursee, Switzerland; 25 g/100 kg per day), a combination of chlortetracycline, sulfadimidine and tylosin (40 g/100 kg per day, CAS 45 K, ufamed AG, Sursee, Switzerland) or a combination of chlortetracycline and spiramycin (30 g/100 kg per day; SK 60, Biokema SA, Crissier, Switzerland) was used over 6–13 days.

Blood analyses

Blood samples were centrifuged within 12 hours after collection and serum was frozen (-80 °C) until further analysis. BRSV antibodies were analyzed using an ELISA (SVANOVIR® BRSV-Ab, Boehringer Ingelheim Svanova, Uppsala/Sweden) in an accredited laboratory (Immunology Unit, University of Veterinary Medicine, Hannover, Germany). The optical density (OD) of the samples and controls were measured at 450 nm in a microplate photometer (Tecan's Infinite® M1000, Thermo Fisher Scientific, Waltham, United States of America). Calculations were performed according to the user manual. Thus, the optical density (OD) value of the sample (OD_{Corr}) was calculated by subtracting the corresponding control ($OD_{Control}$). The mean OD for the negative and the positive controls were calculated. To calculate the Percent Positivity Value (PP), the corrected OD of the sample and the negative controls were divided by the OD of the corrected positive control and multiplied by 100. PP < 10 were considered as antibody negative, PP ≥ 10 were classified as BRSV antibody positive.

For the quantitative measurement of haptoglobin in the serum, a sandwich ELISA (ab137977 Haptoglobin Bovine ELISA Kit, abcam®, Cambridge, United Kingdom) was used. The serum was diluted (1 : 100 000) to ensure an appropriate measurement of the haptoglobin, as the test is originally used for urine or cell culture supernatants. The optical density (OD) of the samples and controls were measured at 450 nm in a microplate photometer (Tecan's Infinite® M1000, Thermo Fisher Scientific, Waltham/United States of America). Calculations were made according to the user manual. For each essay a standard curve was generated from the standard concentrations and the OD values of the standard samples. The best-fit line was determined by regression analysis. The standard curve was used to determine the serum concentration of haptoglobin in ng/ml.

Statistics

Statistical analyses were performed using RStudio® (Version 2026.04.0 Build 526; Posit Software, PBC, Boston, MA, USA) with R statistical software. The packages nlme, car, emmeans, dplyr and janitor were used for data analysis and data preparation. Due to small numbers in some groups (< 5), Fisher's Exact Test was used to compare seroconversion rates between vaccination groups where appropriate.

Repeated measurements of haptoglobin concentrations were analyzed using linear mixed-effects models (lme, package nlme). Vaccination group, sampling time, breed type, sex, fattening farm and batch were included as fixed effects, while calf ID was included as random effect. An autoregressive correlation structure of order 1 [AR(1)] was used to account for repeated measurements within calves. Because residuals showed a skewed distribution, haptoglobin concentrations were log-transformed prior to statistical analysis. Estimated marginal means are presented for interpretation. Performance and slaughter traits were analyzed using linear models. Vaccination group, breed type, sex, fattening farm and batch were included as fixed effects. Age at arrival was included as covariate where appropriate. Estimated marginal means were calculated using the emmeans package and pairwise comparisons between vaccination groups were adjusted according to Tukey.

Antibiotic treatment variables were analyzed using linear models for continuous outcomes and generalized linear models with binomial distribution for binary outcomes. Vaccination group, breed type, sex, fattening farm and batch were included as fixed effects. Frequencies of specific diagnoses were compared descriptively using Pearson's Chi-squared test or Fisher's Exact Test where appropriate.

The mortality was evaluated descriptively; no formal statistical comparison between vaccination groups was performed.

Results are presented as estimated marginal means (EMM) ± standard error (SE) unless otherwise stated. Statistical significance was declared at $p < 0,05$ and trends at $0,05 \leq p < 0,10$.

Results

Out of 488 calves arriving at the veal farms, 70 calves (14,3 %) were excluded due to clinical symptoms. The remaining 418 calves (85,7 %) were included in the study (230 male and 188 female calves). Dairy calves accounted for 191 animals, 227 calves were beef crossbred type. At day 1, the calves were on average 40,7 (± 0,6; SEM) days old and weighed 75,4 (± 0,4) kg.

Mortality

Nine out of the 418 calves enrolled in the study died during the fattening period (2,2 %). The losses were evenly distributed across the vaccination groups. In each of the five groups, two calves died except group KV/KV, in which only one calf died. The prevailing reasons for mortality were BRD (n=5) and abomasal ulceration (n=4). Among the 70 calves which were not enrolled in the vaccination study due to clinical disease at arrival, the mortality was markedly higher (4 out of 70 calves; 5,7 %).

Blood analyses

Already on the day after arrival on the veal farm (day 1), in 191 out of 223 sampled calves BRSV antibodies were found in the serum indicating a seroprevalence of 85,7 %. Seroconversion took place throughout the following 4 weeks in 20 out of the remaining 32 calves. In the groups of calves vaccinated with live and/or killed vaccine, 57–90 % of the calves being seronegative at day 1 seroconverted, but only one out of 6 calves (17 %) in the placebo group (Table 3). The global analysis revealed a significant difference between the groups ($p = 0,028$). Pairwise comparisons showed that LV/KV-calves had a significantly higher seroconversion rate compared to the placebo group ($p = 0,005$). Differences for groups LV/LV, KV/LV and KV/KV compared to the placebo group did not reach statistical significance.

Table 3: BRSV seroconversion in seronegative calves on day 1 after vaccination on day 1 and day 21 according to different protocols. Bold numbers indicate a statistical difference between the protocols.

Vaccination protocol	Calves tested [n]	BRSV negative calves on day 1 [n]	BRSV positive calves on day 28 [n]	Calves with sero conversion [%]
LV/LV	46	7	4	57
LV/KV	45	10	**9**	90
KV/LV	44	4	3	75
KV/KV	42	5	3	60
P/P	46	6	**1**	17

BRSV = bovine respiratory syncytial virus; LV = live vaccine; KV = killed vaccine; P = placebo.

Mean serum haptoglobin concentrations ranged from 0,53 to 1,01 g/L (Table 4). Concentrations did not differ between the vaccination groups ($p = 0,391$). Sampling day affected serum haptoglobin concentrations ($p = 0,041$), with significant higher concentrations observed on day 21 ($p = 0,004$) and day 28 ($p = 0,029$) compared to day 1. Farm ($p < 0,0001$) and batch ($p = 0,0001$) significantly affected serum haptoglobin concentrations, whereas breed type and sex had no significant effect.

Table 4: Estimated marginal mean haptoglobin serum concentrations (±SEM) of calves on days 1, 3, 21 and 28 after arrival on the veal farm vaccinated according to different protocols.

Vaccination protocol	Calves [n]	Day 1 [g/L] ± SEM	Day 3 [g/L] ± SEM	Day 21 [g/L] ± SEM	Day 28 [g/L] ± SEM
LV/LV	39	0,69 ± 0,10	0,81 ± 0,10	1,05 ± 0,10	0,89 ± 0,10
LV/KV	38	0,58 ± 0,10	0,71 ± 0,10	0,94 ± 0,10	0,78 ± 0,11
KV/LV	40	0,54 ± 0,10	0,67 ± 0,10	0,90 ± 0,10	0,74 ± 0,10
KV/KV	38	0,53 ± 0,10	0,65 ± 0,11	0,89 ± 0,11	0,73 ± 0,11
P/P	40	0,58 ± 0,10	0,71 ± 0,10	0,94 ± 0,10	0,78 ± 0,10

LV = live vaccine; KV = killed vaccine; P = placebo

Treatments

Antibiotic treatments did not differ between vaccination groups (Table 5). Oral group therapy using amoxicillin was performed in all farms and batches after arrival. In case of more than 20 % calves of the group suffering from fever, all calves of the group received a second oral group treatment (Supplement 4). Approximately 39 % of the calves received an individual parenteral antibiotic treatment. The proportion of individually treated calves did not differ between vaccination groups (p = 0,644). However, it was affected by veal farm (p = 0,001), batch (p = 0,007) and sex (p = 0,004), i. e., male calves were treated more often than female calves.

Table 5: Antibiotic treatments of calves vaccinated according to different protocols during the fattening period on four Swiss veal farms.

Vaccination protocol	LV/LV	LV/KV	KV/LV	KV/KV	P/P
N	**83**	**82**	**84**	**80**	**89**
Oral group metaphylaxis after arrival [days]	6,7	6,2	6,6	6,6	6,6
Second oral group treatment [days]	9,6	9,6	9,6	9,7	9,7
Total oral group treatment [days]	16,3	15,8	16,2	16,3	16,3
Individually treated calves [n]	33	29	34	38	35
Individual treatment [%], EMM	38,4	34,4	36,9	46,3	36,9
Individual treatment duration [days], EMM ± SE	3,1 ± 0,5	2,4 ± 0,5	2,8 ± 0,5	3,5 ± 0,5	2,7 ± 0,4
Individual treatments					
Pneumonia [T/n]	31/26	24/21	26/24	32/29	30/27
Otitis media [T/n]	10/9	13/12	12/11	14/13	12/12
Diarrhea [T/n]	–	–	1/1	2/2	2/2
Omphalitis [T/n]	1/1	2/2	–	1/1	1/1
Total antibiotic treatment days per animal [days], EMM ± SE	19,4 ± 0,5	18,8 ± 0,5	19,1 ± 0,5	19,8 ± 0,5	19,2 ± 0,5

LV = live vaccine; KV = killed vaccine; P = placebo; EMM = estimated marginal mean; SE = standard error; T = number of treatments; n = number of calves treated individually.

Bronchopneumonia was the predominant indication for individual antibiotic treatment, followed by otitis media (Table 5). The frequencies of pneumonia (p = 0,427), otitis media (p = 0,806), diarrhea (p = 0,165) and omphalitis (p = 0,586) did not differ between vaccination groups.

The duration of individual antibiotic treatment was not affected by vaccination group (p = 0,532), breed type (p = 0,183) or sex (p = 0,065), but differed between veal farms (p < 0,001) and batches (p < 0,001). Similarly, the total number of antibiotic treatment days per calf was not affected by vaccination group (p = 0,652), breed type (p = 0,548) or sex (p = 0,221), but was affected by fattening farm (p < 0,001) and batch (p < 0,001). Adjusted mean total antibiotic treatment days ranged from 18,8 to 19,8 days per calf across vaccination groups.

Performance data

The average daily weight gain (DWG) between day 1 and day 28 after arrival averaged 1,157 kg/day (Table 6). Vaccination group had no significant effect on DWG during this period (p = 0,605). Moreover, neither breed type (p = 0,177) nor sex (p = 0,381) affected DWG between day 1 and day 28. Age at arrival significantly affected DWG during the first 4 weeks of fattening (p < 0,001); for every additional day of age at arrival, calves gained approximately 6 g more per day between day 1 and day 28. Farm also affected DWG during this period (p < 0,001), whereas batch had no significant effect (p = 0,338).

The duration of the fattening period averaged 106 days and was not affected by vaccination group (p = 0,944), breed type (p = 0,070) or sex (p = 0,147). Age at arrival affected the duration of the fattening period (p < 0,001), with older calves having a shorter fattening period. Farm (p < 0,001) and batch (p < 0,001) also significantly affected the fattening period.

The DWG between day 1 after arrival and slaughter averaged 1,472 kg/day. DWG was not affected by vaccination

Table 6: Performance data of calves vaccinated according to different protocols on four Swiss veal farms.

Vaccination protocol	LV/LV	LV/KV	KV/LV	KV/KV	P/P
N	83	82	84	80	89
Age on day 1 [days]	41,4 ± 13,3	41,6 ± 12,3	38,9 ± 11,6	40,1 ± 11,1	41,7 ± 12,7
Weight on day 1 [kg]	75,7 ± 8,2	75,6 ± 8,4	75,0 ± 8,3	74,5 ± 7,5	76,3 ± 8,7
Mortality [n / %]	2 / 2,4	2 / 2,4	1 / 1,2	2 / 2,5	2 / 2,2
DWG day 1–28 [g/day]	1115 ± 37	1109 ± 37	1179 ± 37	1138 ± 38	1162 ± 36
Fattening period [days]	106,9 ± 1,2	105,6 ± 1,2	106,5 ± 1,2	106,5 ± 1,3	106,8 ± 1,2
Carcass weight [kg]	125,7 ± 1,5	128,0 ± 1,5	129,5 ± 1,5	128,6 ± 1,5	126,3 ± 1,4
DWG day 1–slaughter [g/day]	1430 ± 27	1490 ± 27	1495 ± 26	1479 ± 27	1443 ± 26

LV = live vaccine; KV = killed vaccine; P = placebo; DWG = daily weight gain. Values for age and weight on day 1 are presented as means ± SD; performance outcomes are presented as estimated marginal means ± SEM

group (p = 0,291) or breed type (p = 0,704). Male calves had a higher DWG than female calves (1,51 *vs.* 1,42 kg/day; p = 0,001). Age at arrival also had a positive effect on DWG between day 1 and slaughter (p = 0,003); for every additional day of age at arrival, calves gained approximately 3 g more per day.

The average carcass weight was 127,3 kg. Carcass weight was not affected by vaccination group (p = 0,314), breed type (p = 0,839) or sex (p = 0,826). However, age at arrival (p = 0,016), farm (p = 0,005) and batch (p < 0,001) significantly affected carcass weight.

Discussion

Study design and limitations

The production system of the veal farms enrolled in this study corresponded essentially to the typical conditions for roughly 70,000 veal calves fattened in groups on a fee basis in Switzerland. The significance of the data presented here is considered to be high as four different veal farms each with three consecutive fattening periods over a period of one year were enrolled in the study. Thereby, we tried to minimize biases potentially caused by seasonal effects, varying farm specific infectious pressure and management factors on the different farms. As a limitation of this study, it was performed as a field study. The advantage was that this design allowed it to enroll several hundred of calves being vaccinated with commercially available vaccines. The low haptoglobin concentrations in the serum of the vaccinated calves indicate that we have also succeeded in not vaccinating any animals with acute infections, in accordance with the manufacturer's instructions. However, the measured haptoglobin concentrations were relatively high compared to reference values from the literature.[16]

It can be considered as a further limitation of this study that on average two oral group medications took place. This may have masked potential differences in the effectiveness of the tested vaccination protocols. Thereby, the evaluation of individual treatments was the only approach to identify differences in respect of use of antimicrobials between the vaccination groups. At the same time, the study design had the advantage of reflecting real-world conditions — including the common practice of conducting one to three oral group medications on veal farms.

Vaccination as a prevention strategy on veal farms

BRD represents the most important cause of morbidity and mortality on veal farms and has enormous impact on animal welfare and the economic outcome of the fattening operation. As a typical factorial disease, the complex interactions between different pathogens,[11] as well as between pathogens and host cells, abiotic factors (such as air quality, housing system), and management factors (e.g., transport stress concomitant with commingling of calves from many dairy farms, stocking density, feeding regime) are decisive for the pathogenesis and the incidence on the farms.[16]

Extensive use of antimicrobials became the prevailing strategy of producers to minimize morbidity and mortality. However, it is now generally accepted that in particular oral group medications exhibit detrimental effects on risk of (multi-)resistant pathogens[12] and cause disturbances of the intestinal microbiome of calves.[29] Nevertheless, many farmers continue to rely on oral group therapies, on the one hand, due to established habits based on years of experience, on the other hand, to minimize the risk of heavy losses in the event of frequent BRD cases. These concerns must be acknowledged considering the very high prices for veal calves and the low profit margins for veal farmers in Switzerland.

In fact, the findings of this study appear to support this view: based on the analysis of key performance indicators from numerous Swiss veal farms, the performance data of the calves were outstanding while the morbidity was quite low. Only gradually other promising approaches are recognized such as improved clinical diagnostics, including sonography.[13,14,19,22]

The increased use of vaccinations is also an alternative approach. Since decades, vaccinations are an acknowledged tool to minimize disastrous effects of infectious diseases in cattle proven to be effective to reduce morbidity and mortality. Although calves are born with an immature, "naïve" immune system, they are considered according to current scientific consensus as immunocompetent, i. e. they are able to produce an effective immunological response after getting in touch with an antigen.[21]

The evidence of vaccination efficacy against BRD is documented and summarized in several excellent reviews.[8,10,30] In many, but not in all experimental studies, benefits for vaccinated calves compared to unvaccinated controls have been reported in respect to clinical symptoms, pathomorphological alterations, shedding of virus, production of specific antibodies and cell-mediated immunity. One reason for inconsistent results is, that the efficiency of vaccines differs between monofactorial infectious diseases (e.g., FMD, blue tongue, BVD) and factorial diseases (e. g., neonatal diarrhea, BRD, mastitis). A robust immunity can be expected for almost all vaccinated animals following vaccination in case of monofactorial diseases. In contrast, the specific effects of vaccination on morbidity, mortality, proportion of relapses, and protection rate of vaccinated animals vary in case of factorial diseases – markedly depending on season, farm, breed, and environmental conditions. One factor that complicates targeted vaccination is the endemic nature of BRSV in Switzerland, as evidenced by the high proportion of seropositive calves upon arrival. This could be due to residual maternal antibodies or to antibodies produced endogenously following either vaccination or exposure to the field virus on the dairy farm.

In fact, the results of this study did not demonstrate a significant effect of any tested vaccination protocol on calf health. This sobering result may be caused by several factors:

An adequate immune response requires a responsive and competent immune system in a healthy organism, i.e., all vaccines are designated for prophylactic use. Clearly, this precondition is not fulfilled under field conditions having in mind that many calves arriving on the fattener unit are stressed and/or already subclinically or clinically suffering from disease. In this respect, a rate of 14 % clinically ill calves upon arrival as found in our study speaks for itself.

The immune response inducing a reliable protection of the vaccinated calf against respiratory pathogens requires time (roughly 2 weeks after the vaccination) and, according to generally accepted dogma, a booster vaccination. Having in mind that most calves tend to suffer from BRD within the first four weeks after arrival on the veal farm, any vaccination on the veal farm seems to be too late. This statement is supported by the results of a study on Belgian veal farms with an approach quite similar to that of our study. The authors reported that the short-term cure rate as determined sonographically immediately after the first group antimicrobial treatment was not influenced by vaccination. Long-term cure rate, on the other hand, as determined at week 10 after arrival, was higher in the vaccinated group compared with the controls.[14] To achieve a robust immunity by vaccination, it appears to be strategically more advantageous to vaccinate calves already at the dairy farm well in advance of their transfer to the veal farm.

Other pathogens (such as *Mycoplasmopsis bovis*[9] and bovine Corona virus (BCoV)[25] may have played an overwhelming role in BRD outbreaks in the veal farms included in this study.

Maternal colostral antibodies can reduce the immunological response in particular after parenteral application of a vaccine in young calves.

As demonstrated in our study and in agreement with the literature, no vaccination protocol conveys an overall convincing solution of BRD on fattening units.[14,20] From the scientific point of view, LV provoke a more intensive immune response (primarily TH1 response and cell-mediated immunity) compared to inactivated vaccines (primarily TH2 response; production of IL-4, IL-6, and IL-10 favoring the differentiation of B-cells to antibody-producing plasma cells while inhibiting the generation of cytotoxic T-cells). This general statement is supported only in part based on a systematic evaluation of published studies. In fact, the difference in clinical efficiency is not convincing comparing parenterally administered live and inactivated vaccines.

During the last years, the immunomodulatory effect of vaccines in addition to the adaptive immune response has been a matter of debate. The relevance of nonspecific effects[1] of vaccinations against BRD is, however, simply unknown until now. Moreover, interactions between stress responsiveness, temperament, and immunity in cattle have been demonstrated.[7]

Conclusions

None of the vaccination protocols tested in this study had a significant effect on calf health and performance parameters. The most likely explanation is that the timing of the vacci-

nation, i. e. the vaccination after arrival on the veal farm, was inappropriate. Instead, a vaccination directly on the dairy farm makes much more sense and became a mandatory precondition for calves intended to be sold in Switzerland in July 2025. However, recognizing BRD as a factorial disease includes that also further frame conditions on the dairy farm (e.g., colostral supply), during marketing (e.g., transport) and on the veal farm need to be considered in order to achieve a maximal positive effect of vaccination. Last but not least, the age of the calf when moved from the dairy farm to the veal farm is important, as older calves can cope with the challenges of rehousing better than younger calves.[16]

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Validation de divers protocoles vaccinaux contre les maladies respiratoires bovines pour les veaux à haut risque vaccinés après leur arrivée dans des élevages de veaux en Suisses

L'objectif de l'étude était d'évaluer l'efficacité de divers protocoles vaccinaux contre la maladie respiratoire bovine (MRB) chez les veaux nouvellement arrivés dans des élevages de veaux de boucherie. Quatre exploitations suisses ont été sélectionnées pour cette étude menée en conditions réelles, chacune comportant trois périodes d'engraissement. Des vaccins disponibles dans le commerce ont été administrés contre le virus respiratoire syncytial bovin (VRSB), le virus parainfluenza bovin de type 3 et, dans certains cas, Mannheimia haemolytica. Les veaux (n = 418) ont été vaccinés le jour de leur arrivée dans les élevages avec soit un vaccin vivant (LV), soit un vaccin inactivé (KV), soit un placebo (P). Au bout de 21 jours, un rappel vaccinal a été administré selon un protocole croisé, ce qui a donné lieu à cinq protocoles de vaccination : LV/LV (n = 83), LV/KV (n = 82), KV/LV (n = 84), KV/KV (n = 80) et P/P (n = 89). Des échantillons sanguins ont été prélevés chez 223 veaux le jour de leur arrivée (jour 1), au jour 3, au jour 21 et au jour 28 afin d'évaluer les anticorps anti-VRSB et le taux d'haptoglobine. Les traitements antibiotiques par voie orale et parentérale ont été évalués, ainsi que les données de performance, en particulier le gain de poids quotidien. La séroprévalence du VRSB au moment de l'arrivée était élevée (86 %). Les résultats n'ont révélé aucune différence significative ni en ce qui concerne le nombre de traitements antibiotiques, ni au niveau des données de performance liées au protocole de vaccination. Il en ressort que, compte tenu des conditions générales, toute vaccination des veaux à leur arrivée dans l'élevage de veaux semble intervenir à un moment inopportun, c'est-à-dire qu'une protection efficace et spécifique contre la MRB ne peut pas être obtenue de cette manière.

Mots clés: MRB, VRSB, PI-3, GMQ, prévention, traitement, vaccination

Validazione dei diversi protocolli vaccinali contro le malattie respiratorie bovine per i vitelli ad alto rischio vaccinati dopo l'arrivo in allevamenti svizzeri di vitelli da carne

L'obiettivo di questo studio era di valutare l'efficacia dei diversi protocolli vaccinali contro la malattia respiratoria bovina (BRD) nei vitelli appena arrivati in allevamenti di vitelli da carne. Sono stati inclusi nello studio, in condizioni di allevamento reali, quattro allevamenti in Svizzera, ciascuno con tre cicli di ingrasso. Sono stati somministrati vaccini disponibili in commercio contro il virus respiratorio sinciziale bovino (BRSV), il virus parainfluenzale bovino di tipo 3 e, in parte, Mannheimia haemolytica. I vitelli (n = 418) sono stati vaccinati il giorno dell'arrivo in allevamento con un vaccino vivo (LV), un vaccino inattivato (KV) o un placebo (P). Dopo 21 giorni è stato somministrato un richiamo secondo un disegno crossover, ottenendo cinque protocolli vaccinali: LV/LV (n = 83), LV/KV (n = 82), KV/LV (n = 84), KV/KV (n = 80) e P/P (n = 89). Sono stati prelevati campioni di sangue da 223 vitelli il giorno dell'arrivo (giorno 1), il giorno 3, il giorno 21 e il giorno 28 per determinare gli anticorpi anti-BRSV e l'aptoglobina. Sono stati valutati i trattamenti antibiotici orali e parenterali, nonché i dati produttivi, in particolare l'incremento ponderale giornaliero. La sieroprevalenza del BRSV al momento dell'arrivo era elevata (86 %). I risultati non hanno evidenziato differenze significative né nel numero di trattamenti antibiotici né nei dati produttivi in relazione al protocollo vaccinale. Si conclude che, date le condizioni di contesto, qualsiasi vaccinazione dei vitelli all'arrivo in allevamento sembra avvenire in un momento inappropriato, ovvero in questo modo non è possibile ottenere una successiva protezione efficace specifica contro la broncopolmonite enzootica (BPE).

Parole chiave: BRD, BRSV, PI-3, IPG, prevenzione, trattamento, vaccinazione

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