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Analysis of breeding strategies against genetic disorders in Austrian Fleckvieh cattle

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ABSTRACT: This study evaluates different breeding strategies against genetic defects in Austrian Fleckvieh cattle in terms of annual monetary genetic gain and discounted profit. Presently, six genetic disorders are published for Austrian Fleckvieh (Simmental) cattle. The allele frequencies vary between 0.5 and 7% in the female population. If all male carriers are erased from the breeding program, both in herdbook cows as well as in planned mating, a 7% loss in annual monetary genetic gain and a 9% reduction in discounted profit can be expected. If carriers are excluded in herdbook cows only, the reduction in annual monetary genetic gain is 2.4% and 3% in discounted profit, respectively. The reduction in genetic gain due to discarding carriers can be compensated by increased use of multiple ovulation and embryo transfer.
Keywords: genetic disorders; breeding strategy; genetic response; discounted profit

Introduction

Recent advances in genomics and consequent monitoring of missing homozygotes (VanRaden et al. 2011) in cattle has offered new possibilities to detect genetic disorders worldwide. So far, hardly any problems concerning genetic disorders were known in Austrian Fleckvieh (dual purpose Simmental). The relatively high effective population size (Ne=160) of Fleckvieh (Pausch et al. 2013) and the low coefficient of inbreeding (app. 2%) might have contributed to minor problems with genetic disorders.

In the middle of the year 2013, the detection of a few calves with abnormities initiated intense research on the detection of genetic disorders in Fleckvieh by Austrian and German breeding and research organisations. Based on 50K SNP chip data, missing homozygote haplotypes based on the approach of VanRaden et al. (2011) were detected. Researchers from Technical University of Munich (TUM) used gene sequencing techniques to verify mutations (Jansen et al. 2013). Haplotype tests and direct gene tests can now verify whether animals are carriers or not for various genetic defects. Presently, six genetic disorders are published for Fleckvieh in Austria. These are: Arachnomelia (A) (Buitkamp et al. 2011), Thrombopathy (TP) (Jansen et al. 2013), Fleckvieh Haplotype 2 (FH2), Dwarfism (DW), ZinkDeficienyLike Syndrom (ZDL) (Jung et al. 2014), and Bovine Male Subfertility (BMS) (Pausch et al. 2014). The syndrome of A is an inherited malformation mainly of limbs, back and head in cattle. TP is a bleeding disorder characterised by impaired blood coagulation. FH2 calves are in most cases normal at birth, but grow very slowly after weaning (nanism). The disease is caused by a mutation in a gene that leads to the autosomal recessive disorder "Fanconi Bickel Syndrome" in humans. Calves with DW have low birth weights and grow very slowly. ZDL-syndrome causes severe suffering because of dermatosis in homozygous animals and is lethal in any case (Jung et al. 2014).

The breeding strategy in conjunction with genetic disorders does not only have an impact on genetic response to selection but is also of interest for consumers in terms of animal welfare and the overall image of the breed. The new genomic possibilities allow deeper insight and enable breeding organizations to prevent damage for the breed at a very early stage. The present paper gives an overview of the recent status of genetic disorders and characteristics and evaluates various breeding strategies for the Austrian Fleckvieh breeding program.

Materials and Methods

Breeding program Fleckvieh AUSTRIA. In 2012 a new genomic breeding program Fleckvieh AUSTRIA was developed and published by the Austrian Federation of Fleckvieh breeders (AGÖF, 2014). The Fleckvieh population comprises 280.000 herdbook cows (HBC). Each year, 60 young bulls (YB) are selected out of 1,200 candidates (CA) for mating 50% of HBC. The ten best progeny tested bulls (PT) are mated with the other 50% of the HBC. For planned matings, 75% of all potential bull dams (BD) are mated with 12 superior YB and 25% with four superior PT bulls (bull sires, BS). In the reference scenario, only 10% of the CA come out of a multiple ovulation and embryo transfer program (MOET).

Assumptions on breed planning. The program ZPLAN (Willam et al., 2008) optimizes selection strategies in livestock breeding using a purely deterministic approach. The gene flow method and selection index procedures constitute the core of the software. It evaluates both the genetic and economic efficiency of breeding strategies.

The criteria for evaluating alternative breeding programs used in this study were: annual monetary genetic gain (AMGG), which is the monetary superiority per year of the progeny of the selected animals after one selection round in the breeding unit; and discounted profit (DP), which is defined as discounted returns minus dis-

counted breeding costs per cow (investment period (yr): 15; interest rates return and costs (%): 0.03; 0.015).

Evaluated breeding strategies. Three different breeding strategies were evaluated. A single defect locus was assumed which has no direct effect on the desired traits. Strategy 1 aims at erasure of the genetic disorders from the population and does not allow the use of carriers at all in HBC and BD; strategy 2 aims at the maintenance of genetic diversity by planned matings of carriers between BD and BS; and strategy 3 aims to compensate the reduced selection intensity resulting from removal of carriers by use of MOET in strategy 2.

Strategy 1. The strategy "erasure" distinguishes between three variants. Variant 0.5 removes 50% of the candidates due to carrier-status of a genetic defect. Variants 0.3 and 0.1 remove 30% and 10% of the candidates due to a genetic disorder, respectively. Carrier are not used for inseminations in herdbook cows and bull dams as well (selection groups YB>HBC and YB>BD).

Strategy 2. The erasure of carriers is only applied in selection group YB>HBC. The three variants 0.5, 0.3 and 0.1 are analyzed.

Strategy 3. Based on the assumptions of strategy 2 and variant 0.5, BD are genotyped and MOET is used to compensate the loss in selection intensity in the selection groups YB>HBC and YB>BD by increasing the number of candidates. It is assumed that BD are genotyped, with the effect of higher reliabilities of the estimated breeding values and a shorter generation interval by 0.5 years.

Population and economic parameters. The Austrian Fleckvieh population was described in Egger-Danner et al. (2012). Similar assumptions and population parameters are used for this study. Assumptions on selection intensities are adjusted to the new breeding program Fleckvieh AUSTRIA (AGÖF, 2014).

Costs. The costs associated with the management of genetic disorders are direct costs, such as losses based on homozygous carriers, costs for monitoring of the genetic defects, which include costs for testing of genetic defects, and indirect costs. Indirect costs are difficult to estimate and are therefore not considered. The costs of losses due to the use of carriers are calculated based on the actual figures on matings in Austrian Fleckvieh. Compared to random matings about 25% less calves being homozygous for the genetic defect can be expected. Losses for FH2, DW and ZDL are calculated with 350 €, as the calf is not marketable. Costs for A are 700 €, as also damage of the cow can be expected in some cases. Based on these figures and the expected number of homozygous carriers in Austrian Fleckvieh, a loss of 300.000 € is assumed for a strategy where no carriers were excluded from inseminations. If all the carriers are excluded from matings, no losses are assumed; for strategies 0.3 and 0.1, 200,000 and 100,000 € are assumed, respectively.

The costs for direct gene tests are about 30-50 € per genetic defect. Haplotype tests are performed in conjunction with the routine genetic evaluation. In the near future, the relevant SNPs for the known genetic disorders will be included in the costumized chip for Fleckvieh and Brown Swiss. Although no extra costs for genetic tests will occur due to the costumized chip in the near future, additional labor is needed for the management of genetic disorders. Therefore 20 € are assumed per selection candidate for testing of genetic disorders. As all selection candidates are genotyped to get genomic estimated breeding values (GEBV), no additional costs for genotyping of males are assumed. As potential bull dams are currently not genotyped, these costs are assumed for strategy 3, where MOET is used. For strategy 3, 600 € per candidate resulting from MOET is assumed. All other costs are assumed as in Egger-Danner et al. (2012).

Results and Discussion

Allele frequencies. Figures 1 and 2 show the allele frequencies of the different genetic defects for males and females by birth year in the Austrian Fleckvieh population. In TP, FH2 and BMS, an increase is observed in the last years. Figures show that strategies to reduce or at least to maintain allele frequencies are recommended.

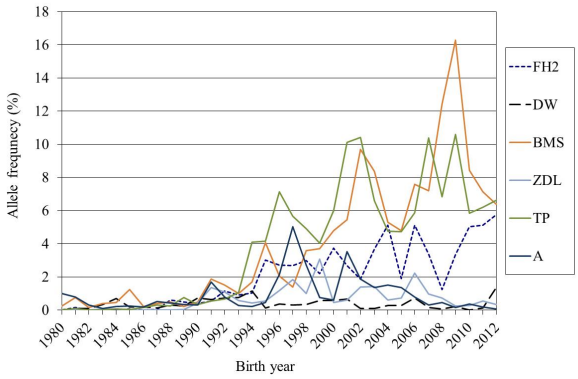

Figure 1: Allele frequencies (%) of males in the Austria Fleckvieh population by birth year

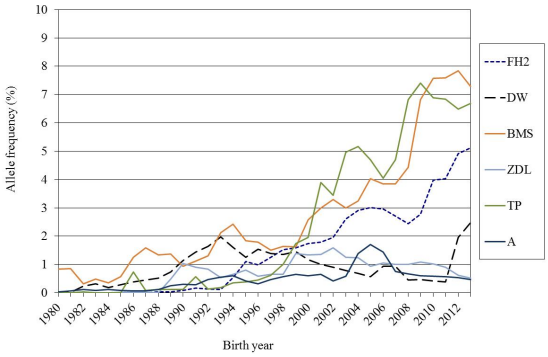

Figure 2: Allele frequencies (%) of females in the Austria Fleckvieh population by birth year

Impact of strategies on AMGG and DP. The results in Tables 1 and 2 are expressed as relative AMGG and relative DP to the reference breeding program Fleckvieh AUSTRIA. The AMGG of the reference scenario is 31.23 €/cow and year and 166.3 €/cow DP. Table 1 shows that the AMGG is reduced by 7.1 percentage points if male carriers are excluded from use in HBC and BD. The DP is reduced by 9.4 percentage points. The results for variant 0.3 and variant 0.1 (30% and 10% of CA excluded from selection) show that the decrease in AMGG can be reduced by 3.5 and 1.0 percentage points; the loss in DP is 4.7 and 1.3 percentage points respectively. The reason for the reduction in genetic response is due to lower selection intensities in the YBs. For strategy 1 and variant 0.5, 120 YB have to be selected out of 1,200 CA, instead of 60 YB in the reference scenario. As indicated in Tables 1 and 2, the selection intensities for YB out of CA and YB>BD (PM) are reduced in the different strategies and variants.

Table 1: Impact of strategy 1 and variants 0.5-0.1 (50%, 30%, and 10% erasure of carriers in HBC and BD) on AMGG and DP, based on Fleckvieh AUSTRIA

	Fleckvieh AUSTRIA	**No use of carriers in herdbook cows and bull dams**		
		variant 0.5	variant 0.3	variant 0.1
AMGG% (€/unit)	100 (31,231)	92.9	96.5	99.0
DP/cow% (€/unit)	100% (166.3)	90.6	95.3	98.7
YB out of CA	60 out of 1200 1:20	120 out of 1200 1:10	85 out of 1200 1:14	66 out of 1200 1:18
PT>HBC	10 out of 57	10 out of 57	10 out of 57	10 out of 57
YB> BD (PM)	12 out of 1200	24 out of 1200	17 out of 1200	13 out of 1200
PT> BD (PM)	4 out of 57	4 out of 57	4 out of 57	4 out of 57

AMGG: annual monetary genetic gain; DP: discounted profit; YB: young bull; CA: genomic tested candidates for selection; PT: progeny tested bull; HBC: herdbook cows; BD: bull dam; PM: planned mating

Table 2: Impact of strategy 2 and variants 0.5-0.1 (50%, 30%, and 10% erasure of carriers in HBC) on AMGG and DP, based on Fleckvieh AUSTRIA

	Fleckvieh AUSTRIA	**No use of carriers in herdbook cows only**		
		variant 0.5	variant 0.3	variant 0.1
AMGG%	100	95.2	97.6	99.3
DP/cow%	100	93.6	97.0	99.4
YB out of CA	60 out of 1200 1:20	120 out of 1200 1:10	85 out of 1200 1:14	66 out of 1200 1:18
PT>HBC	10 out of 57	10 out of 57	10 out of 57	10 out of 57
YB> BD (PM)	12 out of 1200	12 out of 1200	12 out of 1200	12 out of 1200
PT > BD (PM)	4 out of 57	4 out of 57	4 out of 57	4 out of 57

Strategy 2 shows that the loss in genetic response can be reduced if carriers are only excluded for the use in HBC (Table 2). For variant 0.5, the difference between strategy 1 and strategy 2 is 2.3 percentage points in AMGG. For variants 0.3 and 0.1, the difference is even smaller. The best would be to use only non-carrier bulls for insemination in herdbook cows. To maintain genetic diversity, carriers should still be used as bull sires (BS) for planned matings with BD. If in addition to strategy 2 variant 0.5, the BD are genotyped, the AMGG compared to the reference Fleckvieh AUSTRIA is 99.2% and the DP is 97.6%. The use of reproduction technologies like MOET can compensate for the reduction in selection intensities that result from genetic defects management. If each CA would be out of MOET, the AMGG could increase by 13.2% when no genetic defect management strategies are applied. If carriers are not used in HBC, the AMGG is still 9.3% higher than for the reference scenario Fleckvieh AUSTRIA. The DP would be 5.2% above the reference.

The impact of different selection strategies on allele frequencies and inbreeding will be analyzed with simulation studies for Austrian Fleckvieh as well.

Conclusions

Austrian Fleckvieh breeding organizations have started early to use the possibilities of genomics to keep genetic disorders at a low level in the population. Although allele frequencies are mostly below 5% for each genetic defect, the breeding strategy is crucial for the overall longterm development of the breed. Recommended strategies have to take the impact of each genetic disorder into consideration. The removal of carriers for insemination of herdbook cows reduces allele frequency. In combination with reproduction technologies and the use of carriers in BD and as BS the genetic response can be maintained. A progressive approach towards genetic disorders assists in avoiding uncontrolled spreading of undesired genes in the population and offers the possibility to explore the full selection potential again after some years of eradication.

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