Divergent selection for digestive disorders in two commercial rabbit lines : response of crossbred young rabbits to an experimental inoculation of Echerichia coli 0103.

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DIVERGENT SELECTION FOR DIGESTIVE DISORDERS IN TWO COMMERCIAL RABBIT LINES: RESPONSE OF CROSSBRED YOUNG RABBITS TO AN EXPERIMENTAL INOCULATION OF *Echerichia coli* 0103.

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ABSTRACT

A divergent selection for digestive disorders, R for resistance and S for sensitivity, based on routine observational data of signs of enteropathy, was carried out in AGP39 and AGP59 commercial lines of the Hypharm breeding company. Two successive batches (B1 and B2) of 178 crossbred animals, 89 R and 89 S, were produced by mating AGP39 well evaluated bucks with AGP59 well evaluated does and AGP39 bad evaluated bucks with AGP59 bad evaluated does, respectively. In each batch, 27 R animals (RC) and 27 animals (SC) were chosen to constitute the control group while 62 R animals (RI) and 62 S animals (SI) were chosen for inoculation. Individual EBV of animals of the RI group and of the SI group was calculated as the mean of their sire and dam's EBV. In each batch, 31 animals with the lowest EBV in the RI group and 31 animals with the highest EBV in the SI group were sorted to constitute the group RRI and the group SSI, respectively.Young rabbits were carried from Hypharm to the INRA Experimental Platform for Infectious Disease (PFIE) just after weaning at 30 days of age. Inoculated rabbits received 10^5 bacteria of the strain LY265, *E. Coli* O103:H2:K-, rhamnose negative (Licois *et al*., 1992), by oral administration, at 37 days of age. All animals were weighed and checked for clinical symptoms just before the inoculation, 2 days, 6 days, 9 days and 13 days after the inoculation. Average daily weight gain was calculated for each interval. Individual mortality was recorded daily. 13 days after inoculation, 9 rabbits of each sub-group were sacrificed to measure pH of the caecal digesta and for caecum and caecum appendix weighing. The impact of the *E. coli* challenge was significant for growth and for the caecum relative weight. Although mortality tended to be higher in sensitive animals than in resistant animals in batch 1 (p=0.12) there was no significant difference between RI and SI groups for cumulative mortality, daily weight gain and caecum measurements. Mortality was significantly lower (p=0.04) in RRI group than in SSI group at day 11, day 12 and day 13 (31.8 %, 34,8 % and 36.6 % vs. 50 %, 5.1 % and 54.7 % respectively). This difference corresponded to 11 animals for each of the 3 periods.

Key words: Rabbit, disease resistance, digestive disorders, divergent selection

INTRODUCTION

The major challenge in breeding for any disease is to find measures of resistance that are practical to undertake and have a genetic component. In a previous study, Garreau et al. (2008) demonstrated that routine observational data on non-specific digestive disorders in a commercial line can be a useful indicator of resistance to disease, the trait appearing to have a significant genetic component. This disease trait has been included in the breeding objectives of two commercial paternal lines of the breeding company Hypharm to improve the resistance to enteropathies. The aim of this study was to compare responses to an experimental infection with an enteropathogenic E. coli *0103* strain of rabbits divergently selected for resistance to enteropathies.

MATERIALS AND METHODS

Selection of sires and dams

Sires and dams of experimental animals were respectively selected in the AGP39 and AGP59 paternal lines, which are used to produce the PS40 crossbred terminal buck, widely used in French rabbit production (Hypharm, La Corbières, Roussay, France). A binary score based on the observed signs of enteropathy during the growing period (35-70d old) was currently calculated since 1999 in each line (Garreau et al., 2008).Rabbits dead or alive with no sign of enteropathy were given a score of 0. Rabbits dead or alive with a sign of enteropathy were given a score of 1. Sires and dams were selected on their estimated breeding value (EBV) for the entheropathy score, estimated by BLUP applied on an animal model. The effects retained in the final model were sex, batch, parity of dam as fixed effects, and additive and common litter environement as random effects. Among 156 AGP39 bucks available at Hypharm, 6 bucks with the highest EBV were selected to create the group S and 6 bucks with the lowest EBV were selected to create the group R. Among 214 AGP59 available does, 22 does with the highest EBV were selected to create the group S and 22 does with the lowest EBV were selected to create the group R.

Management and measurements of experimental animals

Two successive batches (B1 and B2) of 178 crossbred animals, 89 R and 89 sensitive S, were produced as explained in the previous section. In each batch, 27 R animlas (RC) and 27 S animals (SC) were chosen to constitute the control group while 62 R animals (RI) and 62 S animals (SI) were chosen for inoculation to E. coli. Individual EBV of animals of the RI group and of the SI group was calculated as the mean of their sire and dam's EBV. Young rabbits were carried from Hypharm to the INRA Experimental Platform for Infectious Disease (PFIE, Tours) just after weaning at 30 days of age. They were placed in A2 isolation units and fed *ad libitum* a commercial pelleted food without any antibiotics. Inoculated rabbits received 10^5 bacteria of the strain LY265, *E. Coli* O103:H2:K-, rhamnose negative (Licois *et al*., 1992), by oral administration, 7 days after their arrival at PFIE. Control and inoculated animals were bred in different rooms. All animals were weighed and checked for clinical symptoms just before the inoculation, 2 days, 6 days, 9 days and 13 days after the inoculation. Average daily weight gain was calculated for each interval. Individual mortality was recorded daily. Thirteen days after inoculation, 9 rabbits of each sub-group were sacrificed for caecum and caecum appendix weighing. Relative weight of full caecum and of caecum appendix were calculated by dividing the weight of each organ by the live weight of animal at day 13. The pH of the caecal digesta was taken immediately after sacrifice, with a glass electrode pH meter.

In each batch, 31 animals with the lowest EBV in the RI group and 31 animals with the highest EBV in the SI group were considered to constitute the group RRI and the group SSI, respectively.

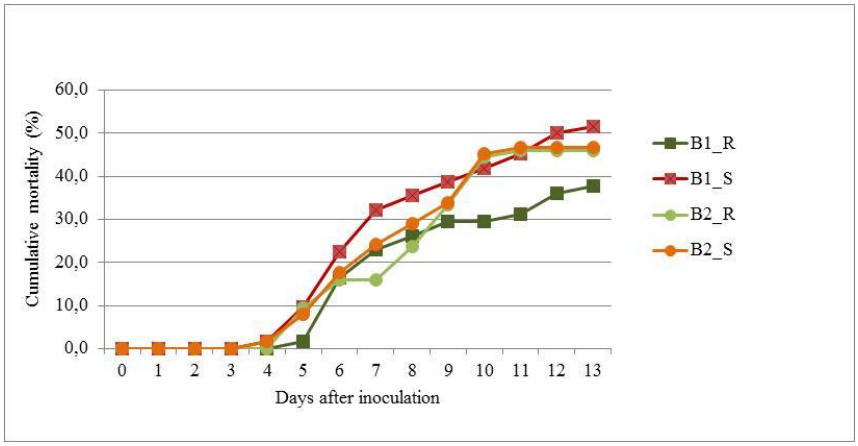
Statistical analyses of traits

The analyses were performed using the SAS software. The GLM procedure was applied for average daily weight gain and caecum measurements. The CATMOD procedure was applied for cumulative mortality. The effects included in the model were the treatment (inoculated, control), the genetic group (R, S) and the batch (B1, B2) for all traits except for cumulative mortality at day 11, day 12 and day 13 in RRI and SSI animals. In this last analyse, the model included only the genetic group effect (RRI, SSI) and the batch effect (B1,B2).

RESULTS

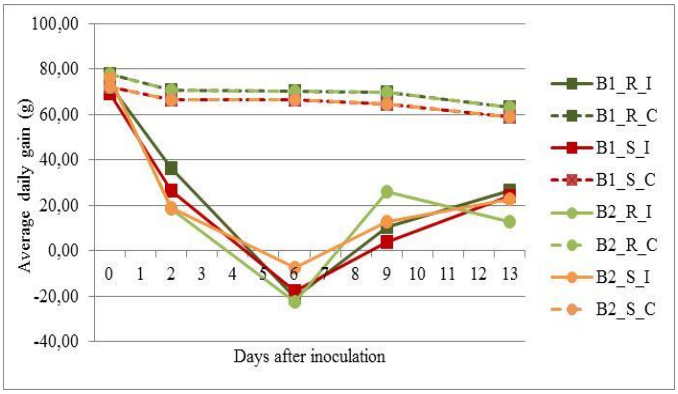
The evolution of cumulated mortality is given in figure 1. There was no mortality in the control group of both batches. Average mortality at day 13 of inoculated rabbit was very similar in the 2 batches (44,7 % vs. 46,4%). Although mortality tended to be higher in S animals than in R animals in batch 1 (p=0.12), there was no significant difference when considering the 2 batches.

Figure 1: Cumulative mortality of selected for resistance (R) and for sensitivity (S) animals in batch 1 (B1) and batch 2 (B2).



The impact of the *E. coli* challenge was significant for growth from 2 to 13 days after inoculation (Figure 2). However, there was no significant difference in growth between resistant and sensitive animals.

Figure 2: Average daily gain of inoculated (I) and control (C), selected for resistance (R) and for sensitivity (S) animals in batch 1 (B1) and batch 2 (B2).



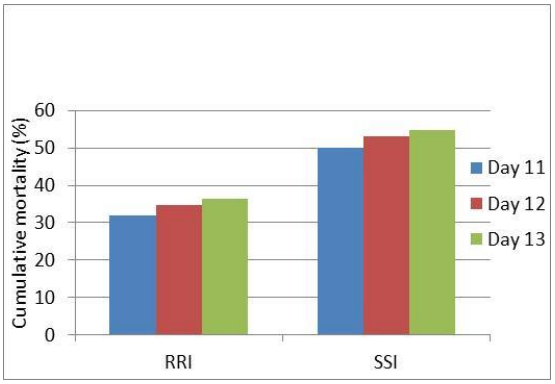
Concerning caecum measurements the effect of inoculation was significant only for the caecum relative weight (Table 1). pH tended to be higher in inoculated animals than in control animals (p=0.09). There was no significant difference between R and S animals for any of these traits.

Table 1: Caecal parameters in inoculated and control, selected for resistance (R) and for sensitivity (S) rabbits, 13 days after inoculation.

	Treatment					
	Control		Inoculated			
	R	S	R	S	Inoculation effect	Group effect
Full caecum weight (% LW)	6.80	7.33	9.82	10.33	***	NS
Appendix weight (% LW)	0.53	0.51	0.57	0.49	NS	NS
pH	6.07	6.22	6.40	6.38	NS	NS

Cumulative mortality of RRI and SSI animals, both inoculated, is given in figure 3. Mortality was significantly lower (p=0.04) in RRI animals than in SSI animals at day 11, day 12 and day 13 (31.8 %, 34.8 % and 36.6 % vs. 50 %, 53.1 % and 54.7 % respectively). This difference corresponded to 11 animals for each of the 3 periods.

Figure 3: Cumulative mortality at day 11, day 12 and day 13 after inoculation in very resistant (RRI) and very sensitive (SSI) rabbits selected on their parents average EBV.



DISCUSSION

The effect of an experimental infection with enteropathogenic *E. coli* O103 strain has been previously described. Gidenne and Licois (2005) and Licois et al.(1992) observed lower mortality rates in conventional rabbits (26 %) and in specific-pathogen free rabbits (10 %) inoculated at 6 weeks of age. However Licois *et al.* (1992) reported a much higher mortality rate in specific-pathogen free rabbits inoculated before 5 weeks of age (over 70 %). In our study the intermediate level of mortality (46 %) seemed to be in agreement with an intermediate age at inoculation (37 days).

Using the same scoring system in the same commercial lines Eady *et al.* (2004) estimated the heritability of incidence of bacterial infection: the reported values (0.04±0.01 with linear model and 0.13±0.04 with a probit threshold model) were close to estimated heritability for resistance to digestive disorders used in the present divergent selection experiment (0.08, Garreau *et al.*, 2008).

Difference between R and S groups was not significant for mortality but it was significant between RRI and SSI groups. Several reasons can explain this result. Sires and dams of experimental rabbits were selected for the incidence of non-specific digestive disorders under natural infection. The selected trait is quite different from the traits measured in this study e.g. a response to an experimental infection with the specific strain LY265, *E. Coli* O103. In other words selection for resistance to

natural and non-specific infection may not be efficient enough to protect animals against an artificial infection or against E. coli itself.
The low genetic response to divergent selection due to a low heritability of the trait and to the single generation of selection may also explain the lack of difference in response to inoculation between R and S animals. The significant difference in mortality between RRI and SSI animals reflected consequently the increase of genetic divergence due to the increase of selection intensity realized by the selection of extreme animals according to their EBV within each group. These results justify continuing the selection on these bases which can be regularly tested with the same infectious model, or may be with another one (ERE, clostridium, coccidia…).

CONCLUSIONS

The response to an experimental infection with an enteropathogenic E. coli *0103* strain of animals divergently selected for resistance to enteropathies was analyzed. A significant difference was observed for mortality between the half most divergent animals only. These results suggest that high selection intensity is required to select for resistance to an artificial infection with E. coli *010.*

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