Relation Between Insect Bite Hypersensitivity And Body Condition Score In Dutch Shetland Mares

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Introduction

Insect bite hypersensitivity (IBH) is the most common allergic skin disease in horses. Prevalence varies from 8% in Swedish born Icelandic horses (Eriksson *et al.* (2008)) and Dutch Shetland mares (Schurink *et al.* (2009)) to 18% in Dutch Friesian mares (Van Grevenhof *et al.* (2007)) and 38% in German Shire horses (Littlewood (1998)). Sensitive horses develop a severe itch after bites of *Culicoides* spp., which results in self-inflicted trauma. The severe itch causes discomfort and disfiguration; welfare of affected horses is seriously reduced. Furthermore, affected horses are often unsuitable for riding or showing purposes and their commercial value is reduced. Severely affected horses are sometimes euthanized (Gortel (1998)). Currently, there is no effective treatment or prevention available. Estimated heritability of IBH is 0.08 on the observed binary scale (Eriksson *et al.* (2008); Schurink *et al.* (2009)).

Many publications support the hypothesis that obesity is a risk factor for allergic diseases in humans (e.g. Thomsen *et al.* (2007), Coogan *et al.* (2009)). Inflammatory cytokines play an important role in both allergic diseases and obesity and have a complicated effect on the immune system. Thomsen *et al.* (2007) suggested that some genes affect both obesity and asthma, although several additional genes influence both disorders independently. Like in humans, an increased production of inflammatory cytokines was observed in obese horses (Vick *et al.* (2007), Adams *et al.* (2009)). Also, inflammatory cytokines production differed between healthy horses and IBH affected horses (Hamza *et al.* (2007), Cunningham and Dunkel (2008)). However, to our knowledge, the relation between body condition and IBH in horses has never been investigated. The aim of our research was therefore to estimate the phenotypic and genetic correlation between body condition score (BCS) and IBH in Dutch Shetland mares.

Material and methods

Material. Data consisted of 7,608 mares with 10,735 observations on IBH scored during foal inspections at home. Mares were scored once a year from June to November by 19 inspectors in the years 2003, 2005, 2006 and 2009. Number of observations per year varied from 1,948 in 2005 to 3,063 in 2003. In total 69.3% of the mares had 1 IBH observation, 21.8% had 2 IBH observations, 7.4% had 3 IBH observations and 1.5% had 4 IBH observations. Number of observations per inspector varied from 16 to 1,400. Solely in 2009 2,809 mares were scored for both IBH and BCS. Average age of mares was 8.4 yr. (range: 2-28). Distribution for withers height category is: 28.6% mini (≤ 86 cm), 22.6% small (87-92 cm), 24.3%

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middle (93-98 cm) and 24.5% tall (99-107 cm). Mares descended from 1,134 sires (1-87 progeny per sire) and 5,333 dams (1-7 progeny per dam).

Trait definition. IBH was scored as 0 (=no clinical symptoms), 1 (=dubious or mild clinical symptoms; e.g. hair loss) or 2 (=clear clinical symptoms; e.g. hair loss, scaling, crusting, bald spots). BCS was scored as underweight (=1), normal weight (=2) or overweight (=3).

Phenotypic relation between IBH and BCS showed a non-linear trend (Figure 2). Univariate analysis of IBH and BCS was done to estimate breeding values and investigate the relation between EBV of IBH and BCS (Figure 1). Negative EBV of BCS did not seem to show a trend with EBV of IBH. However, when EBV of BCS was positive, EBV of IBH increased. Because of among other things computational considerations, underweight and normal weight were for now grouped together and resulting BCS were analyzed as a binary trait.

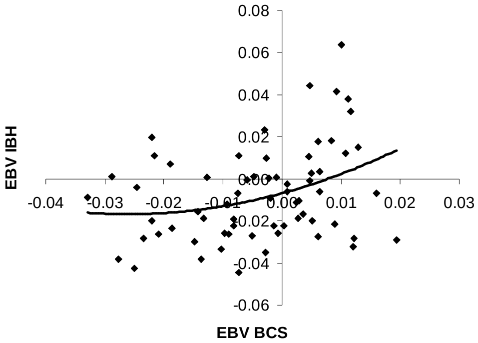

Figure 1: Relation between estimated breeding value (EBV) of body condition score (BCS) and EBV of insect bite hypersensitivity (IBH) from sires with ≥10 progeny

Statistical analyses. Fixed effects were estimated using the procedure GLM (IBH) or GLIMMIX (BCS) (SAS Institute, Cary, NC). An effect was considered to be significant when p-value < 0.05. Shetland pony breeding in the Netherlands is regional and inspectors score regionally. Both region and inspector were excluded from the model, although significant, as preliminary analysis indicated that both effects capture genetic variation.

The linear model for IBH was: $y_{ijklm} = \mu + \text{yearmonth}_i + b_1 \times \text{climate}_l + \text{habitat}_j + \text{WHC}_k + \text{pe}_l + \text{sire}_m + e_{ijklm}$, where y_{ijklm} = the IBH score; μ = population mean; yearmonth_i = the fixed combined class effect of year and month of scoring (i = 1, 2, 3, …, 21); b_1 = the regression coefficient of the continuous covariable climate (climate_l); habitat_j = the fixed class effect of habitat (j = 1, 2, 3, …, 9); WHC_k = the fixed class effect of withers height category (k = 1, 2, 3, 4); pe_l = the random permanent environmental effect of the lth mare (l = 7,608) with $\sim N\left(0, \mathbf{I}_{pe}\sigma^2_{pe}\right)$; sire_m = the random genetic effect of the mth sire (m = 1,134) with $\sim N\left(0, \mathbf{A}\sigma^2_s\right)$, where **A** is a matrix of additive genetic relationships among all Shetland ponies considering 4 generations of pedigree; e_{ijklm} = the random residual error with $\sim N\left(0, \mathbf{I}_e\sigma^2_e\right)$. The threshold model for BCS was: $\eta_{ijk} = \mu + \text{month}_i + \text{WHC}_j + \text{sire}_k$, where η_{ijk} = the linear predictor for BCS; μ = population mean; month_i = the fixed class effect of month of scoring (i = 1, 2, 3, …, 6); WHC_j = the fixed class effect of withers height category (j = 1, 2, 3, 4); sire_k = the random genetic effect of the kth sire (k = 674) with $\sim N\left(0, \mathbf{A}\sigma_s^2\right)$, where **A** is a matrix of additive genetic relationships among all Shetland ponies considering 4 generations of pedigree. An inverse logit link function was used with $\sigma_e^2 = \pi^2/3$.

A bivariate sire model was used to estimate heritability of IBH and BCS, repeatability of IBH and phenotypic and genetic correlation between IBH and BCS using the ASReml program (Gilmour *et al.* (2006)), where phenotypic variance of IBH was $\sigma_s^2 + \sigma_{pe}^2 + \sigma_e^2$, phenotypic variance of BCS was $\sigma_s^2 + \sigma_e^2$ and additive genetic variance was $4\sigma_s^2$.

Results and discussion

Observed IBH and BCS. In total 7.6% of the mares showed IBH clinical symptoms; observed IBH prevalence varied from 4.1% in 2009 to 9.5% in 2005. In total 90.2% (n=2,535) of the mares had a normal weight, 5.2% (n=146) were underweight and 4.6% (n=128) were overweight. Percentage of mares with dubious or mild and clear IBH clinical symptoms increased in underweight and especially overweight mares compared to mares with normal weight (Figure 2). However, negative EBV of BCS did not seem to show a trend with EBV of IBH (Figure 1). Therefore, more research using more data and possibly non-linear models is needed to investigate whether a relation exists between underweight and IBH.

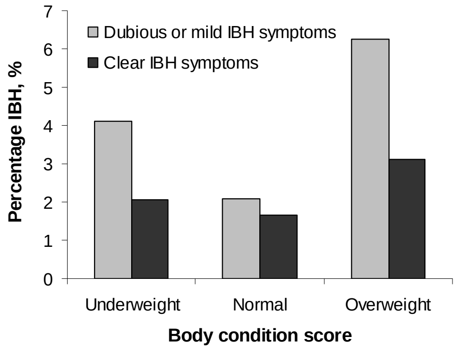

Figure 2: Observed phenotypic relation between insect bite hypersensitivity (IBH) and body condition score

Genetic parameters. Estimated genetic parameters of IBH and BCS are shown in Table 1. Repeatability of IBH was 0.38±0.02. Estimated heritability of IBH agrees with results from Eriksson *et al.* (2008). Heritability of BCS is somewhat higher compared to BCS heritability estimates in literature.

Table 1: Estimated genetic parameters in Dutch Shetland mares$^{\alpha}$

Trait	Insect bite hypersensitivity	Body condition score
Insect bite hypersensitivity	0.05±0.02	0.39±0.37
Body condition score	0.03±0.01	0.38±0.23

$^{\alpha}$ Heritabilities (± s.e.) on diagonal; phenotypic correlation below and genetic correlation above diagonal.

The genetic correlation between IBH and BCS is positive, although with a large standard error. However, a similar genetic correlation between IBH and BCS was found in a dataset containing ~20,000 BCS scored during linear assessment separated in time (year(s)) from IBH scoring. The estimated genetic correlation indicates that IBH and BCS share genes, although most likely additional genes affect both conditions independently. Thomsen *et al.* (2007) found a significant genetic correlation between asthma and obesity in females (r_g=0.28; 0.16-0.38). Also, Hallstrand *et al.* (2005) showed that a considerable part of the covariance between asthma and obesity is caused by shared genes. Based on several findings from genetic studies in humans it is clear that basic functions aimed at metabolism and immune system are common to both obesity and asthma (Thomsen *et al.* (2007)). Similar mechanisms might contribute to the relation between IBH and BCS in Dutch Shetland mares.

Conclusion

Our results show that IBH and BCS are heritable traits in Dutch Shetland mares. The positive genetic correlation between IBH and BCS indicates that both conditions seem to be influenced by common genes in the same direction. A higher genetic predisposition for IBH is therefore associated with a higher genetic predisposition for overweight.

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