The Veterinary Journal 202 (2014) 274–278

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Heritability of epistaxis in the Australian Thoroughbred racehorse population

B.D. Velie [a,*], H.W. Raadsma [b], C.M. Wade [a], P.K. Knight [c,1], N.A. Hamilton [a,1]

[a] Faculty of Veterinary Science, University of Sydney, Camperdown, Sydney, New South Wales 2006, Australia
[b] ReproGen-Animal Bioscience Group, Faculty of Veterinary Science, University of Sydney, Camden, New South Wales 2570, Australia
[c] Discipline of Biomedical Science, Sydney Medical School, Lidcombe, New South Wales 2141, Australia

ARTICLE INFO

Article history:
Accepted 11 June 2014

Keywords:
Epistaxis
Equine
Genetic
Haemorrhage
Heritability

ABSTRACT

Post exercise epistaxis, the manifestation of a severe form of exercise-induced pulmonary haemorrhage (EIPH), has been observed in many equine racing populations. Although multiple analyses have suggested that non-genetic factors may lead to the development of this condition, relatively little consensus has been reached regarding its genetic aetiology. The objective of this study was to provide insight into both genetic and non-genetic factors that may contribute to the expression of epistaxis in the Australian Thoroughbred racing population. Racing records and reported epistaxis occurrences were acquired for 117,088 horses entered in races and official barrier trials from 1 August 2000 until 22 February 2011.

Heritability was estimated using two different logistic generalised linear mixed models (lifetime epistaxis risk $h^2 = 0.27$ and individual race epistaxis risk $h^2 = 0.50$). Sex, age, and year of birth were shown to be significant; however, trainer, jockey, race distance, condition of the track (i.e. 'going'), racecourse, track surface, number of race starters, year and month of race were not significant. Evidence suggests genetic and non-genetic links to EIPH expressed as epistaxis.

Introduction

Exercise-induced pulmonary haemorrhage (EIPH) is characterised by haemorrhage in the lungs attributed to intense physical exertion and has been reported in many Thoroughbred racing populations (Pascoe et al., 1981; Takahashi et al., 2001; Weideman et al., 2003; Hinchcliff et al., 2005; Newton et al., 2005). In severe cases, the condition can manifest as epistaxis, the appearance of blood from the nostrils, and in some instances has been associated with sudden death (Platt, 1982; Gelberg et al., 1985; Johnson et al., 1994; Boden et al., 2005). Despite a documented history of epistaxis in many equine racing breeds (Pfaff, 1950, 1976; Speirs et al., 1982; Gelberg et al., 1985), relatively little is understood about its genetic aetiology. However, evidence suggests that epistaxis manifests as a consequence of EIPH, a condition caused by pulmonary capillary stress failure (West and Mathieu-Costello, 1994). While this evidence may help to explain the pathogenesis of epistaxis, genetic and non-genetic factors leading to the development of this condition are not fully understood.

Our knowledge to date suggests that the aetiology of epistaxis is likely to be highly complex, requiring a specific combination of factors to be present for the condition to be expressed (Cook, 1974; West and Mathieu-Costello, 1994; Takahashi et al., 2001; Weideman et al., 2003, 2004; Hinchcliff et al., 2005; Newton et al., 2005; Langford et al., 2013). However, results from previous studies examining the role of non-genetic factors such as age, track condition and season of year are not uniform and strongly suggest the presence of genetic factors in the expression of epistaxis (Takahashi et al., 2001; Weideman et al., 2003; Hinchcliff et al., 2005; Newton et al., 2005; Langford et al., 2013).

It is possible that certain environmental triggers acting on horses with a specific genetic predisposition for EIPH result in epistaxis. The aim of the present study was to explore this idea in the Australian Thoroughbred racing population by providing insight into both genetic and non-genetic factors that may contribute to the expression of epistaxis. We establish a heritability estimate for epistaxis using the second largest Thoroughbred racing population in the world and provide information on differences in racing careers between horses with reported episodes of epistaxis and the rest of the Australian racing population (Australian Racing Board, 2012a).

Materials and methods

Epistaxis data

Information on all horses with at least one reported episode of epistaxis between August 1999 and February 2011 in Australia was supplied by Racing Information Services Australia (RISA). The data were collected by the authorities for purposes

* Corresponding author. Tel.: +61 2 9351 4789.
E-mail address: brandon.velie@sydney.edu.au (B.D. Velie).
[1] Shared senior authorship.

http://dx.doi.org/10.1016/j.tvjl.2014.06.010
1090-0233/

of implementing clauses related to epistaxis in the Australian Rules of Racing. In Australian racing, epistaxis is defined as the presence of visible blood at both nostrils in the absence of any injury or other identifiable factor that could have resulted in haemorrhage (Australian Racing Board, 2012b). Epistaxis occurrences are generally reported by official veterinarians or racing stewards; however, some trainers will also report the names of horses that experience epistaxis during training.

A horse which, in the opinion of the stewards or an official veterinarian, has suffered an attack of epistaxis shall not without permission of the stewards: be trained, exercised or galloped on any racecourse for a period of 2 months or start in any race for a period of 3 months upon which it must first perform a satisfactory gallop of at least 1000 m in the presence of a steward. If a horse suffers more than one attack of epistaxis it is from then on ineligible to start in any race in Australia (Australian Racing Board, 2012b).

In order to prevent the classification of horses that may have experienced epistaxis prior to August 1999 as non-bleeders (i.e. with no reported cases of epistaxis), the data were filtered to include only horses that were born on or after 1 January 1998. Records contained the date when epistaxis occurred, the state and the age of the horse at the time.

Performance and pedigree data

Performance data for all horses entered in races and official barrier trials from 1 August 2000 until 22 February 2011 were provided by RISA. An official barrier trial is a practice race run under the supervision of the stewards, and is under the same regulatory control as a race; however, the horse and rider are not expected to do everything necessary to win (Australian Racing Board, 2012b). Data from jump-outs were also included where available. A jump-out is defined as a trial, other than an official trial, organised, supervised and controlled by a club or the management of a recognised training track, which is started from barrier stalls, and is conducted in accordance with any conditions set by the Principal Racing Authority (Australian Racing Board, 2012b).

Each individual record corresponded to a specific race or official trial and included RISA horse code, horse name, foal date, sex, sire name, dam name, maternal grandsire name, trainer, race/trial/jump-out date, jockey, track name, track surface, track surface condition, and race distance.

Complete pedigree data for all horses dating back to the foundation sires were provided by the Australian Stud Book (ASB). Pedigree depth was 42 generations and consisted of 522,772 horses.

Summary statistics

Data were structured for analyses using custom scripts written in Perl v 5.1 and statistical analyses were performed using the statistical package R (R Development Core Team, 2011). For horses reported as having experienced epistaxis, summary statistics for career length (CL), number of career starts (NCS), age at first episode of epistaxis (AFE), CL before first episode of epistaxis (CLBE), and NCS before first episode of epistaxis (NCSBE) were calculated. Career length was defined as the time, in months, between an individual's first race, trial, or jump-out in Australia and last race, trial, or jump-out in Australia. Horses with only one race, trial, or jump-out were given a career length of 1 day (0.03 months). The number of career starts was defined as the total number of races, trails and jump-outs in Australia for each individual.

Horses born after 1 January 1998 that raced in Australia between 1 August 2000 and 22 February 2011 with no reported occurrences of epistaxis were considered negative controls for expressing epistaxis (i.e. number of epistaxis occurrences = 0). The career length for these horses was also calculated. All horses were then assessed for their reported number of epistaxis occurrences (0, 1, 2).

Heritability and standard error estimation

Analysis 1

Lifetime risk of epistaxis was treated as a single non-repeated occurrence taken over the entire length of a horse's racing career (epistaxis reported or epistaxis not reported) and analysed as a binary threshold trait using a logistic generalised linear mixed animal model in ASReml-R (R Development Core Team, 2011). Heritability was calculated as:

$$h^2 = \sigma^2_A/(\sigma^2_A + \pi^2/3)$$

with the residual variance represented by $\pi^2/3$. The model included sex and year of birth as fixed effects, while horse was included as a random effect. Sex classifications were based on the sex recorded for the most recent race in each horse's lifetime, as this was believed to be the most informative for a trait encompassing a horse's entire racing career. Information on age at castration was not available. Only fixed effects with a Wald-test $P < 0.05$ were retained in the final model.

Analysis 2

Individual race risk of epistaxis was treated as a repeated occurrence with each race considered as an independent measurement for an occurrence of epistaxis (i.e. for each race: epistaxis reported or epistaxis not reported). Again, epistaxis was analysed as a binary threshold trait using a logistic generalised linear mixed animal model in ASReml-R (R Development Core Team, 2011). The model included sex, age on race day, race distance, barrier number, number of race starters, trainer, jockey, track, surface, track condition, weight carried, and year_month of race as fixed effects and covariates. Horse and permanent environment were included as random effects. Only fixed effects, random effects, and covariates with a Wald-test $P < 0.05$ were retained in the final model.

Univariate survival analyses

A Kaplan–Meier survival curve, stratified by the number of epistaxis occurrences reported (i.e. 0, 1, 2) was produced for CL using the statistical package R (R Development Core Team, 2011). According to Velie et al. (2013), <1.5% of horses in Australia return to racing after not racing or trialling for 2 years. For this reason, horses that raced or participated in an official trial or jump-out within 2 years of 22 February 2011 were considered to potentially still be racing and thus were considered to be right censored. However, in Australia, horses incurring two episodes of epistaxis receive a lifetime ban from racing in Australia (Australian Racing Board, 2012b). As such, the CL for these horses were not considered right censored.

Results

Population data

Records for 117,088 horses, corresponding to 1,852,912 individual performance records, were analysed. A total of 2474/117,088 (2.1%) horses with at least one reported episode of epistaxis were identified. There were 715 sires represented with a minimum, median and maximum of 1, 2, and 42 offspring per sire respectively (interquartile range [IQR] 1–4). There were 2361 dams represented with a minimum, median, and maximum of 1, 1, and 3 offspring per dam, respectively (IQR 1–1). The sample consisted of 277 (11.2%) intact males, 880 (35.6%) females and 1317 (53.2%) geldings.

Summary statistics

A total of 1470/2474 (59.4%) horses raced again after their first episode of epistaxis. Of these, 439/1470 (29.9%) were reported for a second episode of epistaxis. Summary statistics of CL, NCS, AFE, CLBE, and NCSBE for horses incurring at least one episode of epistaxis, stratified by sex, are shown in Tables 1 and 2.

Heritability analysis 1

Heritability of lifetime epistaxis in the Australian racing population, analysed as a single non-repeated occurrence taken over the entire length of a horse's racing career, was 0.27 ± 0.02. Additive genetic variance for lifetime epistaxis was 1.204. Sex and year of birth were shown to be significant ($P < 0.001$).

Heritability analysis 2

Heritability of individual race epistaxis in the Australian racing population, analysed as a repeated occurrence measured during each race, was 0.50 ± 0.01. Additive genetic variance for individual race epistaxis was 3.274. The sex and the age of the horse on the day of the race were significant ($P < 0.001$). All other fixed effects and covariates were not significant and were subsequently dropped from the final model. The effect of permanent environment was also not significant and was subsequently dropped from the final analysis.

Univariate survival analyses

The career lengths of 48,588 (non-bleeders $n = 47{,}860$; bleeders $n = 728$) horses were considered to be right censored (Fig. 1).