Journal of Equine Veterinary Science xx (2016) 1–8

Contents lists available at ScienceDirect

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com

Original Research

Efficacy and Safety of a Commercial Fresh-Frozen Hyperimmune Plasma in Foals With Failure of Passive Transfer of Immunity

Freccero Francesca*, Mariella Jole, Lanci Aliai, Cotignoli Chiara, Castagnetti Carolina

Department of Veterinary Medical Sciences, Alma Mater Studiorum—University of Bologna, Ozzano dell'Emilia, Bologna

ARTICLE INFO

Article history:
Received 20 May 2016
Received in revised form 24 August 2016
Accepted 25 August 2016
Available online xxxx

Keywords:
Neonate
FPT
Fresh-frozen plasma
Sepsis

ABSTRACT

In foals more than 12 hours old, the only effective therapy for the treatment of failure of passive transfer (FPT) of immunity is transfusion of equine plasma. Use and efficacy of equine plasma for prophylaxis and treatment of sepsis, a condition primarily associated with FPT, are widely reported. However, plasma- and recipient-related factors associated with extent of IgG transfer and catabolism are not completely defined. Efficacy and safety of transfusion of a commercial fresh-frozen hyperimmune plasma were evaluated in hospitalized foals younger than 7 days of age with total or partial FPT. Sixty-two foals, classified as affected by FPT only, septic (infection plus systemic inflammatory response syndrome [SIRS]), and nonseptic sick, were included, and serum IgG concentration was measured at admission and 24 hours after plasma transfusion. In 25/62 foals, IgG level after 72 hours was also determined. The impact of different classification criteria for septic foals on IgG transfer was evaluated. Serum IgG measured 24 hours and 72 hours after plasma transfusion was significantly greater than at admission, but no significant difference was found in transfer efficacy (TE) between FPT, FPT septic, and FPT nonseptic foals and no significant difference was found in IgG concentration comparing foals with total and partial FPT or survivors and nonsurvivors. No significant difference was found comparing IgG concentration between bacteremic and nonbacteremic foals and foals with or without SIRS. No foal experienced adverse reactions to plasma transfusion. IgG TE and catabolism did not result significantly affected by the presence of sepsis or illness or by the outcome.

1. Introduction

Due to the epitheliochorial structure of the equine placenta, foals are born immunocompetent, but with an almost absent serum IgG concentration [1]. Equine colostrum is rich of IgG and IgG (T) and, to a lesser extent, IgM and IgA [2,3]. Maximum efficacy in the absorption of immunoglobulins from colostrum occurs at birth, and then falls to 22% just 3 hours later, and down to less than 1% at 20 hours of life. Already after 12 hours of life, in fact, the cells of the small intestine are no longer able to absorb colostral immunoglobulins due to gut closure [1,4]. Many factors can influence the correct passive transfer and can be divided into three groups: missing, reduced, or delayed colostrum intake; ingestion of colostrum of poor quality; and insufficient absorption [1,5]. Foals that do not ingest or do not absorb a sufficient quantity of colostral antibodies, incur in failure of passive transfer (FPT) of immunity, which can be diagnosed by the measurement of serum IgG. Several techniques have been developed as screening tests for the measurement of serum IgG concentration in neonatal foals, and many of these assays are now commercially available as kits: zinc sulfate turbidity, glutaraldehyde coagulation, latex agglutination, enzyme immunoassays, and turbidimetric immunoassays [6]. The immunoturbidimetric

* Corresponding author at: Freccero Francesca, Department of Veterinary Medical Sciences, Alma Mater Studiorum—University of Bologna, via Tolara di Sopra 50, 40064 Ozzano dell'Emilia, Bologna, Italy.
E-mail address: francesca.freccero2@unibo.it (F. Francesca).

0737-0806/$ – see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jevs.2016.08.019

method has already been demonstrated as an accurate quantitative measurement compared to the standard radial immunodiffusion method [6,7]. If the foal nurses for the first time within 2 hours of birth, the serum IgG concentration shows a peak between 18 and 24 hours of life; therefore, the assessment of the passive transfer of immunity must not be performed before this time [8]. Total FPT is defined as a serum IgG concentration <400 mg/dL at 24 hours of life. FPT is defined as partial when the foal reaches a serum IgG concentration between 400 and 800 mg/dL. A value of IgG >800 mg/dL is an index of an adequate passive transfer of immunity [1].

Results of several studies indicate an association between FPT and bacterial sepsis, mostly caused by primary gastrointestinal and pneumonic infections, especially in foals with IgG <400 mg/dL [9–12]. Scientific evidence supports the use and efficacy of equine plasma in the prophylaxis and treatment of septicemia in foals [10,12–14]. A retrospective study, covering 65 cases of septicemia in foals, showed that the transfusion of plasma at admission was significantly associated with survival [10].

The only effective therapy for the treatment of FPT in foals more than 12 hours old is transfusion of equine plasma. The volume of plasma necessary to raise a sufficient concentration of serum IgG cannot be established with precision, as it depends on many variables, including the severity of the FPT, the quantity of IgG contained in the plasma, the weight of the foal, and any ongoing infections. In general, the recommended initial dose for a 45-kg foal is 20 mL/kg, which corresponds to approximately 1 liter of plasma [15–17].

Commercial products generally have an IgG concentration between 1,500 and 2,500 mg/dL. In a 45-kg foal, one unit of plasma (950 mL) containing 1,500–1,700 mg/dL of IgG increases the serum concentration by approximately 200–300 mg/dL. If the administered plasma contains a quantity of IgG ≥2,500 mg/dL, the IgG concentration of the foal can also increase by 400–800 mg/dL. One to three units of plasma may therefore be needed in a foal with total FPT [1]. Immediate or delayed adverse reactions can be associated with plasma transfusion. These can be mild to severe, including itching, edema, urticaria, tachycardia, tachypnea, hyperthermia, behavioral changes, colic, and signs of hemolysis during or immediately after the transfusion, up to anaphylactic shock [18].

There are many reports regarding use of plasma treatment for FPT comparing otherwise healthy foals and septic foals [11,13,14,19,20], but there are no uniform study protocols and foremost classification criteria for sepsis.

The purpose of this study was to evaluate the efficacy and safety of the transfusion of a commercial fresh-frozen hyperimmune plasma (PlasmaLife) in septic and nonseptic sick foals with spontaneous FPT and to compare the impact of different inclusion criteria for sepsis on IgG transfer.

2. Materials and Methods

2.1. Animals and Inclusion Criteria

Foals less than 7 days old hospitalized at the Equine Perinatology Unit (EPU) "Stefano Belluzzi" of the University of Bologna from 2011 to 2015, presenting with partial (400 > IgG<800 mg/dL) or total (IgG<400 mg/dL) FPT and surviving at least 24 hours after the transfusion of the first plasma unit, were included in the study.

Foals were divided into three groups: FPT foals, FPT and septic sick foals (FPT septic), FPT and nonseptic sick foals (FPT nonseptic), on the basis of a complete clinical examination performed at admission/birth, hematological and biochemical examinations, determination of the IgG concentration (if the foal was at least 18 hours old), and blood culture [21].

FPT foals were born from mares referred to the EPU for attended delivery or orphan foals hospitalized for nursing care, which were clinically normal except for FPT.

Foals were classified as septic in the presence of both infection and systemic inflammatory response syndrome (SIRS) [21]. Infection was confirmed on the basis of positive blood culture, positive culture of samples from local sites of suspected infection, or on the basis of postmortem examination. SIRS diagnosis was made as suggested by Wong and Wilkins [22]. Classification based on sepsis score [23] was not enrolled in our analysis.

In FPT nonseptic group, foals hospitalized at the Unit and affected by other neonatal diseases were included.

For subsequent analysis, all FPT sick foals included in the study were also differently classified in bacteremic and nonbacteremic on the basis of blood culture positivity and in foals with SIRS and without SIRS.

All foals were treated with a commercial hyperimmune plasma (PlasmaLife, Siena, Italy). Foals that failed to gain an IgG concentration >800 mg/dL after the first plasma transfusion received supplemental transfusions if permitted by owners. Other treatments during the hospitalization varied case by case based on the existing condition.

The foals were monitored throughout the hospitalization period by a clinical examination performed every 6–12 hours, depending on the severity of existing conditions. The outcome of the foals was described as survivors at discharge or nonsurvivors. Survival rates for each classification group of sick foals were also calculated.

2.2. Evaluation of Serum IgG

The DVM Rapid Test (Value Diagnostics, Spring Valley, WI), a turbidimetric immunoassay, was used to determine the IgG concentration [6]. The concentration of serum IgG was measured on admission (IgG_0) if the foal was at least 18 hours old or 18 hours after birth. The IgG concentration was then evaluated 24 hours (IgG_{24}) and also 72 hours (IgG_{72}) after the end of the last plasma transfusion. For foals receiving multiple transfusions was considered for analysis the IgG determination at 24 hours and 72 hours after the end of the last transfusion. For foals that had not ingested colostrum (because of lacking production by the mare, maternal rejection, death of the mother immediately after delivery, or failure to reach the quadrupedal stance), the serum IgG concentration was considered to be equal to 0.

The IgG transfer efficacy (TE) was calculated for each foal with the following formula, as modified from Wilkins