

Equine Haler – Inhalation device

The Equine Haler is an inhalation device, which has been developed specifically for accurate administration of pharmaceuticals to horses with inflammatory respiratory diseases including chronic obstructive pulmonary disease (recurrent airway obstruction—RAO). The Equine Haler is a convenient method of administering all available types of metered dose inhalers (MDI) to horses. The MDI delivers the medicine at a suitable particle size (< 5 microns) for direct distribution to the small airways. Equine Haler has been developed in Denmark and tested at the Centre for Equine Studies, Animal Health Trust, Newmarket, UK.

One treatment takes 1–2 minutes.

Recommended dosages for aerosol use in horses

Inhaled steroid

Flutide/Flixotide® (Fluticasone propionate) inhalation aerosol 250 µg/actuation. CFC Free: 120 actuations
Recurrent airway obstruction (RAO): 7–8 actuations once or twice daily for a period of 2–3 weeks
When corticosteroids are administered it may be worth considering ending treatment over a few days with an incrementally decreasing dose.

Long-acting beta₂-agonist

Serevent® (Salmeterol) inhalation aerosol 25 µg/actuation. 120 actuations
Recurrent airway obstruction (RAO): 8 actuations once or twice daily for a period of 2–3 weeks

Short-acting beta₂-agonist

Ventolin® (Salbutamol) inhalation aerosol 100 µg/actuation. Free: 200 actuations
Recurrent airway obstruction (RAO): 5–10 actuations 2–3 times daily for a period of 2–3 weeks

Mast cell stabiliser

Lomudal/Intal® (Sodium Cromoglicate) inhalation aerosol 1 µg/actuation, 10 actuations once or twice daily
If necessary the treatment can be extended to one month or longer.

For further information see alternative product recommendations and dosage-recommendations in EQUINE VETERINARY EDUCATION (1999) 11 (3) 124–130, but please note that: the clenbuterol dose, which is said to be milligrams, should be micrograms, and the beclomethasone dose 1320 mg/kg is in some cases better at lower doses.

Doping rules

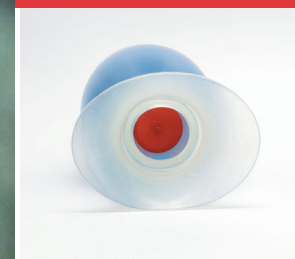
Please check doping restrictions and minimum withdrawal period.



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EQUINEHALER



J-844

EVALUATION OF A NEW SPACER DEVICE FOR DELIVERY OF DRUGS INTO THE EQUINE RESPIRATORY TRACT



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INTRODUCTION

Pulmonary inflammatory disorders occur commonly in the horse. Systemic administration of corticosteroids may be associated with adverse sequelae.

Delivery of drugs directly into the affected airways may improve local drug concentrations as well as reducing systemic uptake.

Inhaled corticosteroids are widely used in the treatment of human inflammatory lung conditions, including asthma and chronic obstructive pulmonary disease.

Equine recurrent airway obstruction (RAO) is characterised by a marked inflammatory response in the presence of aeroallergens, such as moulds.

Nebulisation of liquid corticosteroid preparations has been used, but a number of spacer devices have been developed to allow administration to horses of metered dose inhalers (MDI) designed for human use.

AIMS

To determine the efficiency of the Equine Haler™ for delivering fluticasone propionate from a metered dose inhaler into the equine lung.

To determine the pulmonary distribution of inhaled fluticasone propionate administered with the Equine Haler™.

MATERIALS & METHODS

GENERAL

6 healthy adult horses and 2 healthy adult ponies were studied. All horses were considered healthy based on TW & BAL cytology & bacteriology, clinical examination, thoracic radiographs and V/Q imaging.

Horses were administered ~3.5 µg/kg of fluticasone propionate labelled with ^{99m}Tc from a new design of spacer (Equine Haler™).

Horses were sedated with romifidine 50 µg/kg bodyweight for imaging.

Sequential overlapping scintigraphic images were obtained of the right caudal lung, right cranial lung, cranial thorax, trachea, and head.

Estimates of the lung border were obtained with ^{99m}Tc-MAA (1 MBq/kg).

Markers containing ^{99m}Tc were placed within each image to allow referencing between images.

LABELLING

A single batch of Flixotide Evohalers (250 µg per actuation) were used.

Radiolabelling was performed as described by Newman *et al* (1999) using a seven stage Anderson Cascade Impactor Mk and a flow rate of 28 l/min.

PSD determined with MDI, actuator and spacer combined.

LABELLING continued

PSD was determined with the MDI, actuator and spacer combined.

Particle size distribution (PSD) was determined on:

- Unlabelled FP
- ^{99m}Tc Labelled FP - low activity
- ^{99m}Tc Labelled FP - high activity

The activity and PSD of each MDI was determined prior to use.

Prior to each use, the count rate per second (cps) per actuation of the MDI was determined at a recorded time for subsequent decay correction to allow quantitative analysis of images.



Figure 1. Equine Haler™ spacer for delivery of pharmaceuticals from metered dose inhalers to horses.

IMAGING

Images were obtained using a large field of view gamma camera fitted with a low energy general purpose collimator.

Acquisition parameters: dynamic acquisition; 128 x 128 matrix; 60 x 2 s frames.

ANALYSIS

Images were analysed using HERMES software (Nuclear Diagnostics Ltd).

All images were motion corrected. Inhalation and MAA perfusion images were registered.



RESULTS

In Vitro Studies

The mean PSD of FP and radiolabel for ^{99m}Tc Labelled FP were found to be similar (Figure 2) indicating that the deposition of the radiolabel within the lungs was likely to reflect that of FP.

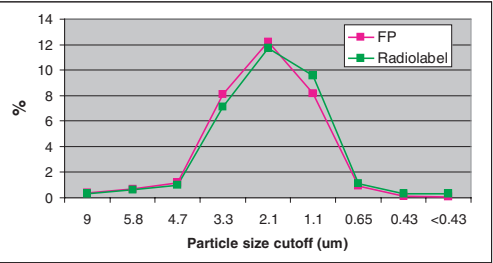


Figure 2. Mean PSD for FP and ^{99m}Tc as a % of total metered dose from ^{99m}Tc labelled FP.

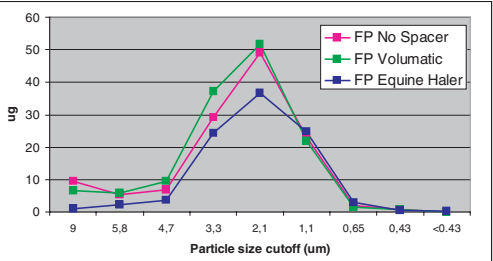


Figure 3. Particle size distribution (µg) of FP delivered from a Flixotide Evohaler with and without a Volumatic spacer (data from Cripps *et al* 2000) and PSD of FP from the Flixotide Evohaler used in conjunction with the Equine Haler™.

The mass of respirable particles (sum of deposition on stages 3 to 5 or 1.1 - 4.7 µm) of FP delivered from the spacer was 96 ± 28 µg (mean ± sd; range 72-127 µg). It was noted that the variation appeared to be related to the angle of the MDI when actuated. It was observed that when the MDI actuator port was not facing directly at the second inspiratory valve that the delivery was low. When care was taken to ensure the MDI actuator port was facing directly at the second inspiratory valve the delivery was always higher.

In Vivo Studies

As expected, there was relatively high deposition of labelled FP around the nostril and upper airways as far as the larynx (Figure 4).

The labelled FP appeared to be distributed throughout the lung according to the distribution of Krypton gas used for ventilation studies. The labelled FP also appeared to reach the periphery of the lung as judged from comparison with images of perfusion obtained with Tc-MAA (Figure 5).

Mean lung deposition for all animals was 8.2 ± 5.2 % of the dose administered (range 2.3 -18.6%).

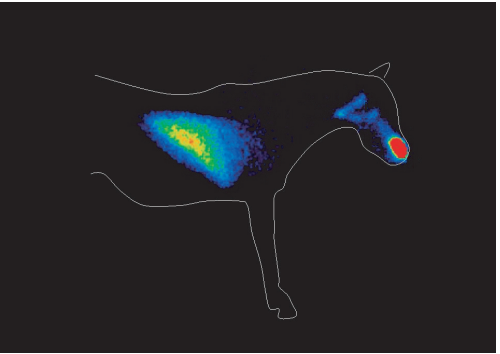


Figure 4. Distribution of ^{99m}Tc-labelled fluticasone propionate after administration of 3.5 µg/kg bodyweight using the Equine Haler.

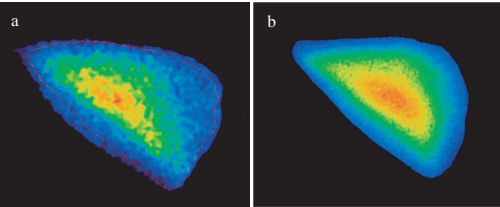


Figure 5. a) Distribution of ^{99m}Tc-labelled fluticasone propionate after administration of 3.5 µg/kg bodyweight using the Equine Haler within the lung of one horse and approximate lung border as determined by subsequent ^{99m}Tc-MAA. b) Example of lung image obtained during inhalation of ^{81m}Krypton gas in a horse with no history of respiratory disease.

DISCUSSION

The Equine Haler appears to achieve an acceptable and even deposition of labelled FP within the equine lung.

Low delivery may be related to the angle at which the MDI is actuated into the spacer.

The Equine Haler was tolerated by all animals after a short familiarisation prior to the study.

REFERENCES

Cripps, A., Riebe, M., Schulze, M. and Woodhouse, R. (2000) *Respiratory Medicine*, 94 (Supplement B), S3-S9.