



Experiences with Parofo[®] (paromomycine) as treatment for *Histomonas meleagridis*

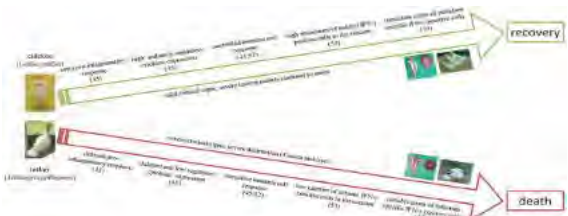
Monita Vereecken

UK 2019-03

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Histomonas meleagridis



Mitra et al., 2018

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FACTS

- Parofo[®] (Paromomycin)
 - Besides AB – also activity **against parasites**

Some Effects of Paromomycin Sulfate on Blackhead in Turkeys

Wallers D, Lindquist, M.S., Sr.D.

AM. J. VET. RES. SEPT. 1989, **23**, 96

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FACTS

- Paromomycin
 - Besides AB – also activity **against parasites**
 - **Binding site** has been demonstrated



Contents lists available at ScienceDirect

Veterinary Parasitology

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

Non-curative, but prophylactic effects of paromomycin in *Histomonas meleagridis*-infected turkeys and its effect on performance in non-infected turkeys

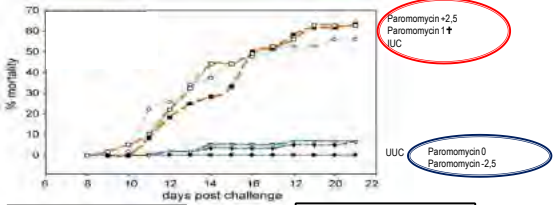
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FACTS



After experimental challenge

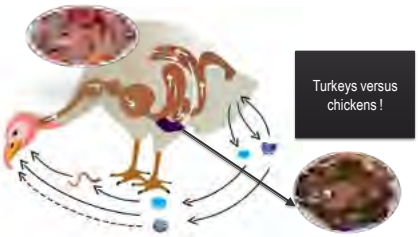
Low Bioavailability

Bleyen et al., 2009 Veterinary Parasitology

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FACTS



Turkeys versus chickens!

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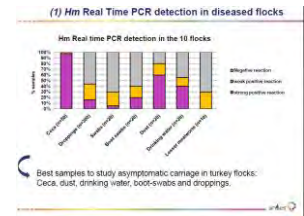


MOST IMPORTANT

Treatment start: as soon as possible !

Early Diagnosis

- PCR sampling
 - Caeca
 - Droppings
 - Dust



Prevalence?

Wide range of carriers



Layers: 89-100% seroprevalence

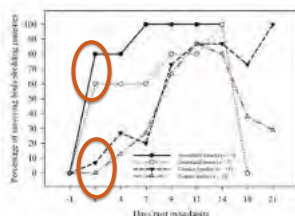
Turkeys: 5.6%

Early Diagnosis

- PCR sampling
- Mortality
 - Early detection
 - Farmer



Shedding after infection



Shedding starts one day pi in majority of the inoculated birds

Shedding in contact birds: one day post infection (1/10)

Farm	Time point	Number and sex of birds	Age of birds at onset of the outbreak	Histomonas specific treatment	Mortality
A	June 2014	7,250 ♂	56 days old	Prologyl® and cangrover	72 % before the slaughter at nine weeks of age
	December 2014	5,200 ♂ 5,000 ♀	From 63 days old	No	125 dead birds before the slaughter at nine weeks of age
	September 2015	15,000 ♀	37 days old	Paralut® 12.5 mg / kg bw for ten days	18 dead birds due to histomoniasis; slaughter at 15 weeks of age
B	November 2014	2,700 ♂ 2,700 ♀	From 27 days old	Prologyl®	200 % mortality in form prior to culling
	September 2016	5,000 ♂ 2,400 ♀	From 18 days old	Paralut® 12.5 mg / kg bw for 12 days	8.3 % in form; 25 dead birds
C	August 2015	5,100 ♂ 6,900 ♀	From 27 days old	Prologyl® for ten days and Paralut® 12.5 mg / kg bw for eight days for ten days	5.3 % in form and 8.5 % in form; 200 % mortality in form prior to culling
D	September 2015	11,500 ♀	48 days old	Paralut® 12.5 mg / kg bw for 5 days	42 %; slaughter at 15 weeks of age
E	September 2016	12,000 ♀	49 days old	Paralut® 12.5 mg / kg bw for 5 days	None
	September 2016	6,200 ♀	34 days old	Paralut® 12.5 mg / kg bw for four days	One dead bird due to histomoniasis

Landman et al., 2015

Sulejmanovic et al., 2017

Testimonial

- „Before the use of Parofo® histomonosis outbreaks almost every time lead to early slaughter or culling of the flocks“
- „Farmers have to perform necropsy on their farms for early detection“
- „Early diagnostics and consecutively early treatment showed best results“

What about...

Dose?

Dose?

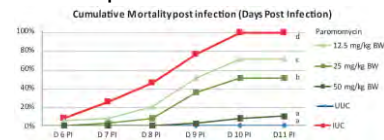
(Minimum) 12.5 mg/kg Body Weight



Dose response in trials (not always!)

Field – Experimental studies

• Dose response



- Models versus reality
- Dynamics in turkey farm?

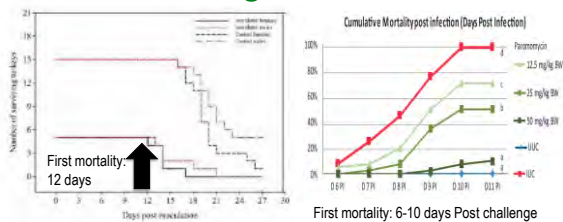
What about...

Treatment duration?

Treatment duration

Minimum 10 days:
evaluate situation

Shedding after infection



Landman et al., 2015

Vereecken et al., 2012



After 10 days

- No more mortality/morbidity? Treatment can be stopped
- Still mortality/sick birds in the flock?
 - It is advised to decrease the dosage to 5 mg/kg body weight and to closely monitor and evaluate the situation on regular base.

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MOST IMPORTANT

Treatment start: as soon as possible !

Which product?

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Product

- Paromomicina Huvepharma
 - Veterinary premix
 - Only product in EU with official claim

4.2 Indications for use, specifying the target species

Pigs (up to 50 kg): enteritis (*E. coli*).
 Pigs: colibacillosis (*E. coli*), salmonellosis (*Salmonella* spp.), necrotic enteritis (*Brochyspira* spp.).
 Broilers: colibacillosis (*E. coli*), salmonellosis (*Salmonella* spp.).
 Rabbits: bacterial enteritis (*E. coli*) except salmonellosis.
 Turkeys: histomoniasis in turkeys caused by *Histomonas meleagridis* when the disease has been diagnosed in the flock.

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Product

- Paromomicina Huvepharma

4.9 Amounts to be administered and administration route

Oral.

Medicated feeding stuff and water consumption depends on the clinical condition of the animals. To obtain the correct dosage, the concentration of paromomycin should be calculated accordingly.

Body weight should be established as correctly as possible in order to avoid under dosing.

Turkeys: 5 mg of active substance/kg BW (equivalent to 714 g of premix /1000 kg of feed) for 6 weeks.



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Product

- Parofo® (WS/OS)
 - Off label use
 - Fast available
 - To be used by veterinarians (no feed mill needed, easier)
 - Older birds: Oral solution more suitable (higher concentrated)

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Product

- **Contra indication:** do not use in turkeys due to the risk of selection for antimicrobial resistance in intestinal bacteria
- Parofo 70 mg/g has via DCP been authorized in the majority of EU Member States in 2014. At the end of the procedure France (as the only MS) insisted on adding the contra-indication based on a study performed in 2008 (Richez 2008, Kempf et al., 2013)

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Product



- In this study turkeys were treated almost lifelong (17 weeks) with paromomycin sulphate (in-feed) at a dose rate of 100 ppm (+/- 5 mg/kg).

Histomonostat versus therapy

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Product

- Resistance development was observed against *E.coli*, *E.faecium* and *S.aureus*.
- The situation returned "back to normal" when the product was withdrawn from the feed (*E. faecium*) or up to one month after withdrawal (*E.coli*).

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Product

- The contra-indication of Parofo[®] is in fact a precaution
- Any use of any antimicrobial in particular used for a relatively long period results in a risk of development of resistance.
- The substantiation of the contra-indication is questionable as it concerns lifelong use versus short application.

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What about use in breeders?

Histomonas alone or in combination with chronic *E. coli*

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What about use in breeders?

Histomonas alone or in combination with chronic *E. coli*

12.5 mg/kg BW for 10 days



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Paromomycin

Pharmacologically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions	Therapeutic classification
Paromomycin	Paromomycin	All food producing species	500 µg/kg 1500 µg/kg 1500 µg/kg 200 µg/kg	Muscle Liver Kidney Eggs	For fin fish the muscle MRL relates to 'muscle and skin in natural proportions'.	Anti-infectious agents/ Antibiotics

- No 0 day withdrawal time for eggs
- No data on hatchability in target species – Trials in non target species + Practical use in the field: **no impact on fertility/hatchability in breeders** (turkey and poultry)

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Conclusion

Our advice for treatment of blackhead with paromomycin sulphate (**Parofor®**) is **12.5 mg/kg body weight for at least 10 days**, after which the situation should be evaluated.

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Summary

- Key point is **to start the treatment as soon as the infection has been established in the flock**
- **Early detection by necropsy and PCR**

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Summary

- Treatment always together with **management measures** in order to slow down the transmission of the parasite
 - Remove as soon as possible the dead birds from the house
 - Cull or isolate all sick and depressed birds
 - If possible make compartments in the house, using separation fences (use different bootcovers for when moving from one to the other compartment)
 - Add frequently fresh litter in the house

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Thank you!

Questions?

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