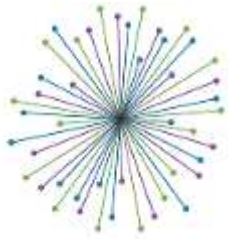

BestBETs for Vets

Supporting veterinary clinicians in making evidence-based decisions

Use of metronidazole in dogs with acute diarrhoea

Clinical Scenario

Mrs Smith brings Horace, a 3 year old male neutered cross breed dog into the clinic because he has had diarrhoea twice overnight and again this morning. During your clinicial exam you find Horace to be bright and alert, you detect no other abnormalities and Mrs Smith reports no signs of haematochezia. Horace's vaccinations are up to date. Mrs Smith is keen to do the best for Horace, and you wonder whether administering metronidazole would lead to a more rapid resolution of clinical signs.....

3-Part Question (PICO)

[In clinically well dogs with acute idiopathic diarrhoea] does [treatment with oral systemic metronidazole compared to no metronidazole] decrease [time to resolution of clinical signs]?

Search Strategy

MEDLINE(R) In-Process & Other Non-Indexed Citations and MEDLINE(R) 1946 to Present using the OVID interface

(dog.mp. OR dogs.mp. OR canine.mp. OR canines.mp. OR canis.mp. OR exp Dogs/)

AND

(diarrhoea.mp. OR diarrhea.mp. OR enteritis.mp. OR loose faeces.mp. OR loose feces.mp. OR loose stools.mp. OR loose stool.mp. OR watery faeces.mp. OR watery feces.mp. OR watery stool.mp. OR watery stools.mp. OR exp Diarrhea/ OR exp Enteritis/)

AND

(metronidazole.mp. OR flagyl.mp. OR MTZ.mp. OR exp Metronidazole/)

CAB Abstracts 1910 to Present using the OVID interface

(dog.mp. OR dogs.mp. OR canine.mp. OR canines.mp. OR canis.mp. OR exp Dogs/)

AND

(diarrhoea.mp. OR diarrhea.mp. OR enteritis.mp. OR loose faeces.mp. OR loose feces.mp. OR loose stools.mp. OR loose stool.mp. OR watery faeces.mp. OR watery feces.mp. OR watery stool.mp. OR watery stools.mp. OR exp diarrhoea/ OR exp enteritis/)

AND

(metronidazole.mp. OR flagyl.mp. OR MTZ.mp. OR exp metronidazole/)

Search Outcome

MEDLINE

- **45** papers found in MEDLINE search
- **43** papers excluded as they don't meet the PICO question
- **0** papers excluded as they are in a non-English language
- **0** papers excluded as they are review articles/in vitro research/conference proceedings
- **2 total relevant papers from MEDLINE**

CAB Abstracts

- **98** papers found in CAB search
- **96** papers excluded as they don't meet the PICO question
- **0** papers excluded as they are in a non-English language
- **0** papers excluded as they are review articles/in vitro research/conference proceedings
- **2 total relevant papers from CAB**

Total relevant papers

2 relevant papers from both MEDLINE and CAB Abstracts

Summary of Evidence

Shmalberg et al. (2019) USA

Title:	A randomized double blinded placebo-controlled clinical trial of a probiotic or metronidazole for acute canine diarrhea
Patient group:	Client owned dogs visiting 2 emergency centres of a University academic teaching hospital. Sixty three dogs were enrolled into one of three groups - administered placebo, metronidazole or a commercially available probiotic.
Study Type:	Randomised controlled trial

Outcomes:

- Survey at presentation to identify influencing factors (e.g. duration of diarrhoea, patient factors such as age, breed etc)
- Blood for complete blood count and serum biochemistry at presentation
- Faecal sample (where possible) at presentation for faecal flotation and a commercial PCR gastrointestinal panel
- Follow up owner phone interviews 5-10 days after initiation of treatment
- Owner recorded days until faeces were considered to be consistent with score of 3 or less on the Waltham Faeces Scoring System
- Survey 6 months after enrollment of last dog to identify if additional diarrhoeic episodes had occurred

Key Results:

- No statistically significant difference in time to achieving acceptable faecal consistency (e.g. score of 3 or less on the Waltham Faeces Scoring System) between the groups given placebo or metronidazole
- After adjusting for factors identified as possibly influencing the results (e.g. history of previous diarrhoea, dietary indiscretion), there was still no statistically significant difference in time to achieving acceptable faecal consistency between the groups

Study Weaknesses:

- No mention of whether there were differences in breed, sex or neuter status between the groups of dogs prior to the commencement of the study
- The authors did carry out a power calculation for the study; it was based on a mean and standard deviation from another study
- Faecal consistency scoring was carried out by owners; no mention was made of whether owners were given training in how to score faecal consistency apart from the provision of a chart
- Eligibility was at the discretion of the attending vet and other treatments could be administered (e.g. fenbendazole) as a way of maximising client enrollment
- A financial incentive was provided to owners to participate in the study which could have biased the sample population
- Results pertaining to the impact of breed, sex or neuter status on the outcome of interest were not reported
- The main aim of the paper was not the main aim of this BestBET

Attachment:

Evidence appraisal (/soe_attachments/574/4147-Critical appraisal - Randomised Controlled Trial Shmalberg_Final.pdf)

Langlois et al. 2020, USA

Title:	Metronidazole treatment of acute diarrhea in dogs: A randomized double blinded placebo-controlled clinical trial
Patient group:	Forty eight dogs visiting Michigan State University Teaching Medical Centre for acute diarrhoea were screened for inclusion.
Study Type:	Randomised controlled trial

Outcomes:

- At presentation, faecal samples were taken for testing for *C.perfringens*
- Owner recorded faecal scoring logs for 7 days; diarrhoea was considered resolved once the animal had 2 consecutive faecal scores less than or equal to 4 on the Bristol faecal scoring system
- On re-presentation at 7 days, further faecal samples were taken
- Dogs in the control group with persistent diarrhoea at day 7 were treated with metronidazole for an additional 7 days, owners continued to keep faecal scoring logs during this time

Key Results:

- Age, sex, weight, maropitant citrate treatment, baseline faecal score or requirement for fluid therapy did not impact on duration of time until resolution of diarrhoea in the linear regression model
- Dogs in the metronidazole group took a mean of 2.1 +/- 1.6 days to achieve resolution of diarrhoea compared with dogs in the control group who took a mean of 3.6 +/- 2.1 days (P=0.04).

Study Weaknesses:

- Groups appeared to be comparable prior to the commencement of the study for most factors, although breed and neuter status does not appear to have been reported
- The faecal scoring system used has been validated in humans but not in dogs previously
- It is unclear how the decision making occurred in relation to the extra treatments that could be prescribed at the clinicians discretion (e.g. fluid therapy, maropitant citrate)
- Outcomes were assessed blind, excluding the second 7 day period where any unresolved diarrhoea in control animals was treated with metronidazole with the owners knowledge
- The data relating to time (days) to resolution of diarrhoea in animals receiving metronidazole appeared to be skewed by an outlier (7 days until resolution of diarrhoea; Figure 1). It is unclear whether this outlier was excluded in the analysis and/or whether it had an influence on the distribution characteristics of the data (normally distributed or not).
- The study was funded by Zomedica, who produce a preparation of metronidazole targeted at acute diarrhoea in dogs. It is unclear whether the company's own preparation was used in the study.

Attachment:

Evidence appraisal (/soe_attachments/574/4148-Critical appraisal - Randomised Controlled Trial Langlois_Final.pdf)

Comments

This is an updated version of the BET originally published in June 2017 authored by Roger Holden and Marnie Brennan. The original BET didn't return any relevant evidence. This version adds 2 new papers and corresponding appraisals.

If the aim of a research trial is to demonstrate equivalence between interventions, then the trial needs to be designed in a different way to one where superiority of one intervention over the other is the aim. The absence of statistical differences can be due to small sample sizes and resulting Type II statistical errors (when there isn't enough power to demonstrate a statistically significant difference). Further research with larger sample sizes would provide more certainty here.

As well as considerations relating to the possible immunomodulatory effects of metronidazole in these cases, thought should be given as to whether using antimicrobials and antiparasiticides is warranted, justified or appropriate, particularly where animals appear clinically well at presentation.

Bottom line

There is currently limited peer-reviewed evidence to support a clinically significant reduction in the time to resolution of clinical signs when metronidazole is used in clinically well dogs with acute idiopathic diarrhoea compared with no treatment.

References

Shmalberg J, Montalbano C, Morelli G, Buckley GJ, (2019). A randomized double blinded placebo-controlled clinical trial of a probiotic or metronidazole for acute canine diarrhea. *Frontiers in Veterinary Science* **6**: doi:10.3389/fvets.2019.00163.

Langlois DK, Koenigshof AM, Mani R, (2020) Metronidazole treatment of acute diarrhea in dogs: A randomized double blinded placebo-controlled clinical trial. *Journal of Veterinary Internal Medicine* **34**: 98-104.

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