BestBETs for Vets

Supporting veterinary clinicians in making evidence-based decisions

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

The effect of intrauterine cephapirin on subsequent fertility in cows with clinical endometritis

Clinical Scenario

During a routine fertility visit you find a lot of cows with white vaginal discharge during post-calving checks at 21-28 days, and you discuss with the farmer the implications of endometritis. After discussing preventative measures for endometritis, and examining the transition cow management, the farmer tells you that when your boss does the routine, he puts a Metricure tube in, to "wash her out and get her in calf quicker". You do not often use Metricure tubes, and wonder whether there is any evidence behind using intra-uterine cephapirin to improve reproductive outcomes...

3-Part Question (PICO)

In [dairy cows with clinical endometritis] does [the use of cephapirin versus nothing] improve [subsequent fertility]?

Search Strategy

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

(cow.mp. OR cows.mp. OR cattle.mp. OR bovine.mp. OR bovines.mp. OR bos.mp. OR exp Cattle/)

AND

(endometritis.mp. OR whites.mp. OR metritis.mp. OR uterine infection.mp. OR uterine infections.mp. OR uterine inflammation.mp. OR uterine disease.mp. OR uterine diseases.mp. OR purulent vaginal discharge.mp. OR metritis.mp.)

AND

(metricure.mp. OR cephapirin.mp. OR cefapirin.mp. OR cephalosporin.mp. OR cephalosporins.mp. OR cefalosporin.mp. OR cefalosporins.mp. OR antibiotic.mp. OR antibiotics.mp. OR exp Anti-Bacterial Agents/)

AND

(fertility.mp. OR fertile.mp. OR gravidity.mp. OR fecundity.mp. OR calving index.mp. OR conception.mp. OR

reproductive performance.mp. OR exp Fertility/)

CAB Abstracts 1910 to Present using the OVID interface

(cow.mp. OR cows.mp. OR cattle.mp. OR bovine.mp. OR bovines.mp. OR bos.mp. OR exp cattle/)

AND

(endometritis.mp. OR whites.mp. OR metritis.mp. OR uterine infection.mp. OR uterine infections.mp. OR uterine inflammation.mp. OR uterine disease.mp. OR uterine diseases.mp. OR purulent vaginal discharge.mp. OR exp uterine diseases/)

AND

(metricure.mp. OR cephapirin.mp. OR cefapirin.mp. OR cephalosporin.mp. OR cephalosporins.mp. OR cefalosporin.mp. OR cefalosporins.mp. OR antibiotic.mp. or antibiotics.mp. OR exp antibiotics/)

AND

(fertility.mp. OR fertile.mp. OR gravidity.mp. OR fecundity.mp. OR calving index.mp. OR conception.mp. OR reproductive performance.mp. OR exp fertility/ OR exp fecundity/ OR exp conception/)

Search Outcome

MEDLINE

- **80** papers found in MEDLINE search
- **69** papers excluded as they don't meet the PICO question
- **5** papers excluded as they are in a foreign language
- **0** papers excluded as they are review articles/in vitro research/conference proceedings
- **4 total relevant papers from MEDLINE**

CAB Abstracts

- **310** papers found in CAB search
- **290** papers excluded as they don't meet the PICO question
- **20** papers excluded as they are in a foreign language
- **0** papers excluded as they are review articles/in vitro research/conference proceedings
- **4 total relevant papers from CAB**

Total relevant papers

5 relevant papers from both MEDLINE and CAB Abstracts

Comments

One systematic review study was found (Lefebvre and Stock 2012; see reference section for more details), however not all papers within the review were relevant to our question, therefore the relevant papers were analysed seperately for the purposes of this BET. There was also a Vet Record paper reporting the original findings of the BestBET, which was also excluded from analysis.

Summary of Evidence

LeBlanc et al, 2002, Canada

Title: The effect of treatment of clinical endometritis on reproductive performance in dairy cows

Patient group: Holstein cows (n=316) diagnosed with endometritis (purulent vaginal discharge or cervical diameter >7.5cm) examined 20-33DIM from 27 herds.

Study Type: Randomised controlled trial

Outcomes:

- Clinical cure (abscence of mucopurulent discharge and cervical diameter <7.5cm) after 14d
- Pregnancy rate
- Calving to service interval
- First serve pregnancy risk
- Calving to pregnancy interval
- Cumulative pregnancy risk
- Number of inseminations per pregnancy
- Removal risk for reproductive failure
- Culling data

Key Results:

- No significant differences in clinical cure after 14 days between treatment and control
- No significant effect of treatment on time to pregnancy
- No significant effect of treatment on pregnancy rate when given 20-26DIM
- Significant effect of treatment on pregnancy rate when treated 27-33DIM in treatment group (63% increase, P=0.01)
- Significant effect of treatment on pregnancy when a palpable corpus luteum present in treatment group (75% increase, P=0.003)

Study Weaknesses:

- Sample size too small to detect small differences in reproductive outcomes
- Blinding was not possible
- Ethical approval not stated
- Missing animals from follow up examinations
- Funded by company which manufactures the treatment

Attachment:

Evidence appraisal (/soe_attachments/561/4098-2936-Critical appraisal - Randomised Controlled Trial LeBlanc 2002a.pdf)

Runciman et al, 2008, Australia

Title: Effect of intrauterine treatment with cephapirin on the reproductive performance of seasonally calving dairy cows at risk of endometritis following periparturient disease

Patient group: Dairy cows (n=222) from 17 seasonally calving herds, with purulent vaginal discharge at 28-37 days prior to mating start date.

Study Type: Randomised controlled trial

Outcomes:
- Hazard ratio for pregnancy

Key Results:

- Pregnancy 'risk' of treated discharge positive cows was 2.09-fold (P=0.013) compared with control cows

Study Weaknesses:

- Cows were examined and treated at a variety of times post calving, frequently within the first 21 days in milk
- Study population was derived from animals at risk of endometritis (i.e. dystocia, twins etc) which is a very specific group of animals, and may not be representative of herd level endometritis diagnosis in practice.
- A large portion of the study was dedicated to analysis of data involving 'at risk' cows rather than those with endometritis, limiting the relevance of this study to our PICO question.
- Funding source not stated, but company that manufactures the product provided product support for the study

Attachment:

Evidence appraisal (/soe_attachments/561/4099-3273-Critical appraisal - Randomised Controlled Trial Runciman 2008a.pdf)

Runciman et al, 2009, Australia

Title: Comparison of two methods of detecting purulent vaginal discharge in postpartum dairy cows and effect of intrauterine cephapirin on reproductive performance

Patient group: 261 dairy cows from 6 seasonal dairy herds examined 7-28 days post calving with purulent vaginal discharge (diagnosed either via metricheck device or visual vaginoscopic examination)

Study Type: Randomised controlled trial

Outcomes:

- Proportion of cows conceived to first service
- Proportion of cows submitted for service within 3 weeks of mating start date
- Proportion of cows pregnant within 6 weeks of mating start date
- Proportion of cows pregnant within 21 weeks of mating start date

Key Results:

- Proportion of cows conceiving to first service were statistically significantly better in the treated group than non-treated group for cows diagnosed with endometritis by vaginal examination (p=0.036), but not for those diagnosed with metricheck (p=0.15)
- Proportion of cows served within 3 weeks of mating start date were not statistically different between treated group and non-treated group for cows diagnosed with endometritis by vaginal examination, or those diagnosed with metricheck (p>0.3)
- Proportion of cows pregnant within 6 weeks of mating start date were statistically significantly better in the treated group than non-treated group for cows diagnosed with endometritis by vaginal examination (p=0.015), and also for those diagnosed with metricheck (p=0.011)
- Proportion of cows pregnant within 21 weeks of mating start date were statistically significantly better in the treated group than non-treated group for cows diagnosed with endometritis by vaginal examination (p=0.026), but not for those diagnosed with metricheck (p=0.082)

Study Weaknesses:

- Study population was derived from animals at risk of endometritis (i.e. dystocia, twins etc) which is a very specific group of animals, and may not representative of herd level endometritis diagnosis in practice.
- Animals were examined and treated as early as 7 days post calving, and although a positive effect of treatment was reported, it is an earlier diagnosis and treatment than commonly seen in UK practice.
- Unclear if blinding was performed
- Required sample size not reached
- Funding source not stated
- Basic data not fully described
- The outcome of interest in our BET was not the primary aim of this study

Attachment:

Evidence appraisal (/soe_attachments/561/4100-3268-Critical appraisal - Randomised Controlled Trial Runciman 2009a.pdf)

Denis-Robichaud, Dubuc, 2015, Canada

Title: Randomized clinical trial of intrauterine cephapirin infusion in dairy cows for the treatment of purulent vaginal discharge and cytological endometritis

Patient group: Holstein cows (n=424) from 28 dairy herds within 250km of St-Hyacinthe (Quebec), with purulent vaginal discharge at 35(+/-7) days in milk

Study Type: Randomised controlled trial

Outcomes:

- Pregnancy rate at first service

Key Results:

- Intrauterine cephapirin increased first service pregnancy 'risk' compared with untreated controls (31.3% vs 15.5%, P<0.01)
- A greater improvement in first service pregnancy 'risk' was seen in cyclic cows (treated cows 34.1%; no treatment 22.7%) than anovular cows (treated cows 26.4%; no treatment 21%)

Study Weaknesses:

- Ethical approval not mentioned
- Some disrepencies between figures in text and tables (i.e. number of animals with purulent vaginal discharge)
- High culling rate prior to pregnancy diagnosis
- Part funded by company which manufactures the treatment

Attachment:

Evidence appraisal (/soe_attachments/561/4101-3270-Critical appraisal - Randomised Controlled Trial Denis-Robichaud 2015a.pdf)

Tison et al., 2017, Canada

Title:	Effectiveness of intrauterine treatment with cephapirin in dairy cows with purulent vaginal discharge
Patient group:	1247 cows from 18 Canadian farms
Study Type:	Randomised controlled trial
Outcomes:	• First service conception rate • Time to pregnancy (up to 300DIM) • Presence of discharge in the vagina • Bacterial growth of vaginal cytobrush

Key Results:

- Cephapirin treatment increased the odds of conceiving at first service (OR = 1.8, CI = 1.2-4.2, P = 0.001) compared with negative control
- Cephapirin treatment reduced the time to pregnancy (HR = 1.42, CI = 1.0-1.8, P = 0.02) compared with negative control, and reduced the median time to pregnancy by 38 days.

Study Weaknesses:

- Blinding not stated
- 70 cows removed from one herd due to failure to follow synchronisation procedure
- All cows were enrolled in a presynch-ovsynch protocol
- Study population was a convenience sample of Canadian cows

Attachment:

Evidence appraisal (/soe_attachments/561/4102-Critical appraisal - Randomised Controlled Trial_Tison et al 2017_Final.pdf)

Comments

This is an updated version of the BET originally published in May 2016.

The original BET included all papers except Tison et al. (2017) which has been added.

There was a wide variety of methods used for the diagnosis of clinical endometritis within these studies. Additionally, the time periods between calving and diagnosis of, and treatments for, purulent vaginal discharge were very variable between the studies. This variability is to be noted and may or may not be relevant to local systems.

Both Runciman papers (2008 and 2009) use an "at risk" population of animals from which to draw a proportion diagnosed as having vaginal discharge. This is different to diagnosing endometritis directly from the whole herd as occurred in the other studies in this BET. Additionally, within these 2 studies, the cows were examined/treated at various times after calving, as early as 7 days post partum, which is again different from the other studies in this BET. This has the potential to affect the relevance of these 2 studies to specific types of clinical approach, particularly those where cows are not usually examined for clinical endometritis until greater than 21 days post-calving.

Whilst cephapirin appears to be effective at improving fertility in animals with clinical endometritis, it is important to consider the judicious use of antibiotics within farm animal practice.

Bottom line

The evidence suggests that cephapirin improves subsequent fertility in dairy cows affected by clinical endometritis, when compared to no treatment.

References

LeBlanc, S.J., Duffield, T.F., Leslie, K.E., Bateman, K.G., Keefe, G.P., Walton, J.S., Johnson, W.H., (2002). The effect of treatment of clinical endometritis on reproductive performance in dairy cows. *J. Dairy Sci.* **85:** 2237–49.

Runciman, D.J., Anderson, G.A., Malmo, J., Davis, G.M., (2008). Effect of intrauterine treatment with cephapirin on

the reproductive performance of seasonally calving dairy cows at risk of endometritis following periparturient disease. *Aust. Vet. J.* **86:**250–8.

Runciman, D.J., Anderson, G.A., Malmo, J., (2009). Comparison of two methods of detecting purulent vaginal discharge in postpartum dairy cows and effect of intrauterine cephapirin on reproductive performance. *Aust. Vet. J.* **87:**369–78.

Lefebvre, R.C., Stock, A.E., (2012). Therapeutic efficiency of antibiotics and prostaglandin F 2α in postpartum dairy cows with clinical endometritis: An evidence-based evaluation. *Vet Clin North Amer: Food Anim Pract*, **28**:79-96.

Denis-Robichaud, J., Dubuc, J., (2015). Randomized clinical trial of intrauterine cephapirin infusion in dairy cows for the treatment of purulent vaginal discharge and cytological endometritis. *J. Dairy Sci.* **98:** 6856–64.

Tison, N. Bouchard, E. DesCôteaux, L. Lefebvre, RC., (2017). Effectiveness of intrauterine treatment with cephapirin in dairy cows with purulent vaginal discharge. *Theriogenology.* **89:** 305-317.

About this BET

First author:
Bobby Hyde
Second author:
Marnie Brennan
Institution:
School of Veterinary Medicine and Science, The University of Nottingham

CEVM, The University of Nottingham

Search last performed:
2020-02-05 19:25:37
Original publication date:
2020-02-27 19:25:37
Last updated:
2020-02-27 19:25:37