VETERINARY EVIDENCE online

In Bitches diagnosed with Pyometra, is Medical Therapy using Antibiosis Alone as Effective as Combining Ovariohysterectomy with Antibiosis in Reducing Morbidity and Mortality?

A Knowledge Summary by

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KNOWLEDGE SUMMARY

Clinical bottom line

Ovariohysterectomy combined with antibiosis is more effective in achieving clinical cure than systemic antibiosis alone. Systemic antibiosis may be associated with recrudescence of the pyometra and the evidence base is weaker for this approach.

Question

In canine bitches diagnosed with pyometra, is systemic antibiotic therapy alone as effective as surgical ovariohysterectomy with systemic antibiosis in achieving clinical cure?

Clinical scenario

You are presented with a 10 year old female entire Staffordshire bull terrier during afternoon consultations. Her owner has noticed that she has been drinking more than usual for around a week now and has also is displaying signs of being in season again, despite her last season being only 6 weeks ago. Based on your clinical examination and a brief ultrasound examination an open pyometra is diagnosed. The owner is keen to do what she can for the dog however finances are limited and would like to know if there is an alternative to surgery. One of the options you consider is the use of systemic antibiosis alone.

Summary of the evidence

Adamovich-Pippe et al (2013)	
Population:	Entire bitches with pyometra.
Sample size:	N=12
Intervention details:	Dogs with confirmed pyometra underwent laparscopic ovariohysterectomy as a treatment.
Study design:	Case-controlled study
Outcome studied:	Was laparoscopic surgery curative?
Main findings: (relevant to PICO question):	• Laparascopic ovariohysterectomy is a valid treatment option for canine pyometra. • Careful case selection is required; iatrogenic organ rupture is a potential complication.
Limitations:	• Small population studied • No long term follow-up on the animals. • No control group used.

Bartoskova et al (2007)	
Population:	Bitches with pyometra undergoing ovariohysterectomy
Sample size:	N=13
Intervention details:	Bitches undergoing treatment for pyometra had blood samples taken immediately before and 7days after ovariohysterectomy
Study design:	Case controlled study
Outcome studied:	Whether haematological parameters and immune function normalised after ovariohysterectomy.
Main findings: (relevant to PICO question):	• Haematological parameters and immune function normalised within 7days of ovariohysterectomy. • Further immunostimulation was not necessary.
Limitations:	• All animals underwent same procedure; could not clarify whether was immunostimulation or if derragements were secondary to systemic inflammation. • No population justification noted.

De Cramer (2010)	
Population:	Entire bitches with pyometra.
Sample size:	N=8
Intervention details:	Dogs with confirmed pyometra were given supportive fluid therapies and antibiosis (Gentamicin and potentiated amoxicillin). They then underwent trans-cervical uterine lavage using 5% povidone-iodine in saline solution, combined with direct visualisation of the uterus.
Study design:	Case control study
Outcome studied:	Whether surgical lavage of the uterus produced more reliable and faster outcomes.
Main findings: (relevant to PICO question):	• E. coli was the most common organism isolated. • Vaginal discharge was scant following the procedure, becoming absent by day4 in all except 1 dog, which resolved after 12days. • All dogs subsequently returned to cyclicity and conceived.
Limitations:	• No set exclusion criteria; any dog presenting with pyometra was accepted. • No case controls used. • Treatment is not licensed and small population means further studies needed before this method could be justified routinely. • Likely expensive as a treatment; benefit over medical therapy uncertain.

Gupta et al (2015)	
Population:	Dogs with pyometra managed with ovariohysterectomy.
Sample size:	N= 9
Intervention details:	All dogs underwent ovariohysterectomy. Uterine pathology findings and surgical success rates are reported.
Study design:	Descriptive case series.
Outcome studied:	The pathological findings in the uterus and ovaries, alongside the success of surgical ovariohysterectomy.
Main findings: (relevant to PICO question):	• All dogs survived surgery with no reported complications. • The authors stated that their success was similar to that previously reported in well known text books, but did not quote any figures. • The use of medical management in particularly ill/ toxaemic animas prior to surgery was thought to be beneficial.
Limitations:	• No statistics used in this study. • No figures are directly quoted; the outcomes of surgery here are very vague and that paper better describes the pathological changes (gross and histological) associated with canine pyometra. • There is no control group to compare the findings too.

Jitpean et al (2014)	
Population:	Bitches diagnosed with pyometra
Sample size:	N= 356
Intervention details:	Bitches presenting to a Swedish hospital with pyometra between 2006-07
Study design:	Retrospective case controlled clinical audit
Outcome studied:	Complications arising from therapy for pyometra
Main findings: (relevant to PICO question):	• 356 dogs in total; 315 treated surgically, 9 medically and 32 were euthansased on presentation. • Post operative mortality 1% (4/315). • 12.4% (40/356) developed peritonitis, 5.3% (19/356) developed urinary tract infection, 2.2% (8/356) developed wound infections. 1.7% (6/356) developed uveitis and 1.4% (5/356) developed arrythmias. • Poorer clinical condition at admission associated with prolonged hospitalisation. • Leucopaenia and abnormal temperature associated with increased risk pyometra. • Antibiosis given pre-admission 21% dogs (65/356) and post-operatively in 35% dogs (124/356). Didn't seem significant as to when antibiotics were given. • Overall complication rate 25%.

Limitations:	• Cases were not controlled at the time of admission; therefore therapeutic protocol not necessarily standardised between animals. • Included animals not receiving surgery in certain statistical calculations; artificially lowers scores. • Most animals received ovariohysterectomy; cannot reliably compare outcomes to medical therapy.

Sen et al (2001)	
Population:	Female entire dogs with open pyometra
Sample size:	N=22 or N=14 unclear
Intervention details:	• All dogs received daily vaginal douching with 50- 150ml 2.5% povidone iodine followed by intra-uterine infusion of Intamox (amoxicillin and dicloxacillin; 20mg/kg). • This was performed for 5- 7 days. • All dogs received Gynomeena liquid, 2- 4 teaspoons a day depending on bodyweight, orally, for 14 days. • Some dogs received 5% dextrose in normal saline, systemic antibiosis and anti-emetics for toxaemia.
Study design:	Descriptive case series
Outcome studied:	Resolution of the clinical signs of open pyometra.
Main findings: (relevant to PICO question):	• All dogs achieved clinical cure in this study, with no recurrence during a one year period. • Within 5- 7 days then palpable uterine diameter reduced significantly. • No vulval discharge was observed after 12 days. • 4 out of 22 dogs conceived after subsequent mating. • The authors concluded that this treatment regime can be adopted with great success.
Limitations:	• The study is not clear with regards to the population numbers; it says 22 initially and then 14 and does not clarify this point. • It is a case series study; no control group and no statistics are performed. • Unknown number of dogs received systemic fluid therapy, antibiosis and anti-emetic therapy. • There is a very limited literature review in this paper, with a textbook being referenced too.

Singh et al (2010)	
Population:	Dogs diagnosed with pyometra
Sample size:	N= 5
Intervention details:	All dogs received intramuscular injection of ceftriaxone sodium and tazobactum sodium for 4- 6 days. Vitamin B injections and meloxicam was also used for supportive treatment.

Study design:	Case series
Outcome studied:	Clinical resolution of the pyometra.
Main findings: (relevant to PICO question):	• All dogs achieved clinical cure in this study; 3 dogs after 4 days treatment and a further 2 dogs after 6 days of treatment. • No dogs experienced recurrence of the pyometra. • The authors recommend that ovariohysterectomy be the choice treatment. • The authors discussed that this medical management was effective only in the "earlier" stages of pyometra.
Limitations:	• This is a case series, so whilst treatment was successful there is no control group to compare the findings too. • Being a case series, no statistical analysis of the results was performed. • Only 5 dogs took part in this study, therefore the significance of the findings should be interpreted with caution. • The paper mentions a lack of recurrence of pyometra, but follow up times are not quoted. • Medications given were mentioned in the study but other supportive measures, such as the need for intravenous fluid therapy, was not mentioned. • Dosages of other medications used was not mentioned. • Long term follow up is not available.

Wallace et al (2015)	
Population:	Dogs diagnosed with open or closed pyometra, or mucometra with a uterine body of less than 5cm in diameter
Sample size:	N=7
Intervention details:	All dogs underwent laparascopic ovariohysterectomy, with diagnosis subsequently beign confirmed with either uterine culture or histopathology
Study design:	Case series
Outcome studied:	Was laprascopic assisted overiohysterectomy a viable technique in the management of canine pyometra or mucometra?
Main findings: (relevant to PICO question):	• 1 dog had conversion to an open approach following the discovery of uterine rupture at the start of surgery. • All dogs survived (100%). • 6 dogs were discharged 1 day later. • Follow-up period ranged from 7- 421 days, with no complications reported. • Median uterine body diameter 2.2cm • Mean age at surgery 68months (range 19-151) • 1 dog was subsequently diagnosed with a macro-follicular granulose cell tumour alongside pyometra (incision extended)

	• 1 dog required a second port to exteriorise uterus. • 1 dog experienced intra-operative loss of pneumoperitoneum. • Mean surgery time was 85 minutes (range 40-110 minutes).
Limitations:	• Case series; not a prospective clinical trial so no comparison of different techniques. • No statistics were used in this descriptive study. • Only 7 dogs form the case series, 1 of which required conversion to an open approach so less frequent complications may not have been encountered. • Wide range of follow-up means not all complications may have been noticed. • Use of concurrent antibiosis not recorded.

Wheaton et al (1989)	
Population:	Entire female dogs diagnosed with pyometra who were managed surgically with ovariohysterectomy
Sample size:	N=73
Intervention details:	Medical records were analysed for all dogs diagnosed with pyometra and treated surgically between January 1976 and April 1987. The diagnosis was confirmed surgically. Some dogs had the diagnosis further confirmed histologically but these observations were not included.
Study design:	Retrospective descriptive study based on case records
Outcome studied:	To discuss the outcome of dogs with pyometra when managed surgically with ovariohysterectomy. It also aims to discuss three particular complications associated with such management.
Main findings: (relevant to PICO question):	• Mean age of affected dogs was 7.9 years. • 6/8 dogs aged <3years had received estradiol cyprionate or megestrol acetate within 6 months of presentation, and one 10yr old bitch. • The mean time since the last observed season was 8 weeks. • The most common bacteria isolated was E. coli (66% cases). • 3 dogs developed post-operative complications related to embolization of septic foci. All dogs survived, but one dog suffered intermittent recurrence of clinical signs which were antibiotic responsive over the next 3 years. • 4 dogs (5%) died either during surgery or in the immediate post-operative period. • Age did not appear to affect outcome in this study.
Limitations:	• Retrospective case study; no control groups. • Diagnosis confirmed based on visual assessment only; early cases or cases with less gross pathological change may have been inadvertently excluded. • No statistical analysis was performed in any of these groups and so associations cannot be clarified.

	• Long term follow up data is lacking. • The paper does not specify that all complications are mentioned; overall data on complication rates is difficult to state here.

Appraisal, application and reflection

Overall, there seemed to be much better quality evidence to support the use of ovariohysterectomy compared to antibiosis alone. That said however, there were no studies which directly compared the two methods. Whilst potentially very useful, such studies would need careful case selection and safeguards given the potential for a detrimental clinical effect. Once available however, a review of the new evidence alongside existing evidence would allow a more definitive comparison of the two protocols to be made. The quality of the current published papers reviewed also means that a bias towards ovariohysterectomy may have been made owing to the increased level of detail that the ovariohysterectomy protocols contained, and the fact that such papers were written more recently.

In the studies themselves, inclusion criteria were often well defined; exclusion criteria were rarely defined though. A substantial number of papers were rejected for review because they focused on different protocols, such as comparing the efficacy of dopamine agonists versus an anti-progestin. Such protocols will be evaluated separately. Unfortunately, several other papers were rejected as they were single case reports. Such reports were not deemed sufficient evidence to support the use of certain treatment protocols.

Whilst systemic antibiosis was advocated in all studies reviewed, there were no studies in which antibiosis alone was evaluated and compared to a control group. It would also be interesting to see studies in which ovariohysterectomy was utilized in non-septic patients and no antibiosis used, which may prove beneficial from the perspective of antibiotic resistance. Ovariohysterectomy appeared to yield good results clinically, with the large majority of cases achieving resolution of the clinical signs.
Statistical analysis was not commonly utilized in the studies evaluated here; primarily because they tended to be case series rather than controlled clinical trials. No studies seemed to include a phrase justifying their sample size either; with many clinical studies involving relatively small study populations. Study recruitment issues may have been factors here.

However, many of the studies did agree on anamnestic factors such as age of presentation. The most frequently isolated organisms were similar where culture and sensitivity was performed (with E. coli being most frequently isolated).

Methodology Section

Search Strategy	
Databases searched and dates covered:	The following search terms were applied to the PubMed database, accessed via the NCBI website (1910-2015) and the CAB abstracts database (1973-2015) accessed on the OVID platform
Search terms:	(dog OR dogs OR canine OR bitch OR bitches) AND (antibio* OR amoxicillin OR sulphona* OR sulfona* OR genta OR ceftriaxone) AND (ovariohysterect* OR ovariehysterect* OR hysterect* OR spey OR spay* OR neuter*) AND (pyometra) AND (treat* OR manag*)
Dates searches performed:	18 January 2016

Exclusion / Inclusion Criteria	
Exclusion:	Articles not available in English, single case reports, book chapters and conference proceedings, articles which were not relevant to the PICO.
Inclusion:	Articles available in English which were relevant to the PICO. Articles had to involve more than one animal and had to describe the protocol used

Search outcome

Database	Number of results	Excluded – study design	Excluded – non English Language publication	Excluded – did not answer PICO question	Total relevant papers
CAB Abstracts	126	2	0	115	9
PubMed	4	0	0	3	1
Total relevant papers when duplicates removed					**9**

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