

CONSERVATIVE MANAGEMENT OF CANINE PYOMETRA. PART II: THERAPEUTIC PROTOCOLS, CLINICAL EFFICACY AND REPRODUCTIVE OUTCOMES

Skliarov Pavlo Mykolayovych

Doctor of Veterinary Sciences, Professor
Dnipro State Agrarian and Economic University, Dnipro, Ukraine
ORCID: 0000-0002-4379-9583
skliarov.p.m@dsau.dp.ua

Vakulyk Viacheslav Volodymyrovych

Candidate of Historical Sciences, Associate Professor
Dnipro State Agrarian and Economic University, Dnipro, Ukraine
ORCID: 0000-0001-8773-2287
vakulik.v.v@dsau.dp.ua

Bilyi Dmytro Dmytrovych

Doctor of Veterinary Sciences, Professor
Dnipro State Agrarian and Economic University, Dnipro, Ukraine
ORCID: 0000-0003-3896-0384
bilyi.d.d@dsau.dp.ua

Mylostyvyi Roman Vasyliovych

Candidate of Veterinary Sciences, Associate Professor
Dnipro State Agrarian and Economic University, Dnipro, Ukraine
ORCID: 0000-0002-4450-8813
mylostyvyi.r.v@dsau.dp.ua

Chekan Oleksandr Mykolaiovych

Doctor of Veterinary Sciences, Professor
Sumy National Agrarian University, Sumy, Ukraine
ORCID: 0000-0002-5676-1947
achekanne@gmail.com

This review synthesises and critically evaluates published evidence on current conservative treatment protocols for canine pyometra, with particular emphasis on their clinical efficacy, recurrence rates and subsequent reproductive outcomes. Particular attention is given to antiprogestins, prostaglandins and dopamine agonists, their combination regimens, and concomitant antimicrobial, fluid and supportive therapies.

Conservative treatment is not universally applicable and requires careful patient selection. It is contraindicated in cases of severe sepsis, uterine rupture, peritonitis and severe renal or hepatic dysfunction. Aglepristone showed high clinical efficacy, with primary recovery rates of 77.1–92.3% using conventional protocols, whereas a modified regimen of 10 mg/kg administered on days 1, 3, 6 and 9 achieved 100% clinical recovery, with no recurrence reported during 24 months of follow-up. Prostaglandin monotherapy achieved reported efficacy rates of 70–100%, although its use may be associated with systemic adverse effects and requires particular caution in cases of closed-cervix pyometra. Combination protocols generally showed favourable outcomes: aglepristone combined with cloprostenol achieved clinical recovery rates of 90–95%, whereas regimens incorporating aglepristone, cloprostenol and cabergoline achieved rates of 95–100%, with reported recurrence rates of 0–5%. Reproductive function could be preserved following successful conservative treatment, with reported pregnancy rates of 80% after aglepristone treatment and 92.14% following combined aglepristone and cloprostenol therapy. Treatment outcomes also depend on adequate control of bacterial infection, endotoxaemia, fluid and electrolyte disturbances and systemic dysfunction. Ultrasonographic monitoring provides an important means of assessing regression of pathological uterine changes following treatment.

Overall, the available evidence indicates that appropriately selected combination pharmacological protocols may provide greater clinical efficacy and lower recurrence rates than the monotherapy protocols reviewed. However, no universally applicable standardised protocol for the conservative management of canine pyometra has yet been established.

Key words: pyometra, bitches, conservative treatment, aglepristone, prostaglandins, cloprostenol, cabergoline, reproductive function, recurrence.

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Introduction. Conservative pharmacological treatment of canine pyometra has evolved in recent years from a largely experimental approach into a well-supported and clinically relevant alternative to surgical treatment (Melandri et al., 2019; Xavier et al., 2023, 2024; Lopes et al., 2025). Although ovariectomy has long remained the definitive treatment of choice for controlling the source of systemic inflammation, the increasing value of breeding animals and the need to preserve their reproductive potential have stimulated considerable interest in fertility-preserving therapeutic protocols (Ros et al., 2014; Contri et al., 2015; Dadona et al., 2023; Lopes et al., 2025). Contemporary pharmacological strategies are directed not only towards evacuation of uterine contents but also towards targeting the progesterone-dependent endocrine and pathophysiological mechanisms underlying pyometra. Accordingly, a major objective of conservative treatment is to restore the functional integrity of the reproductive tract while preserving the bitch's subsequent reproductive capacity (Contri et al., 2015; Melandri et al., 2019; Da Rosa Filho et al., 2021; Lopes et al., 2025).

Conservative treatment protocols have evolved from the use of natural and synthetic prostaglandins (PGF_{2α}), whose clinical application has been constrained by pronounced systemic adverse effects and considerable variability in long-term outcomes, towards progesterone receptor antagonists (antiprogestins) and dopamine agonists, which have broadened the therapeutic options for medical management while improving the prospects for preservation of reproductive function (Ros et al., 2014; Melandri et al., 2019; Da Rosa Filho et al., 2021; Lopes et al., 2025). Aglepristone competitively blocks progesterone receptors, thereby facilitating cervical opening, evacuation of pathological uterine contents and regression of uterine lesions, and consequently creating favourable conditions for preservation of reproductive function (Fieni, 2006; Rosa Filho et al., 2020; Da Rosa Filho et al., 2021; Dadona et al., 2023).

Despite the growing body of evidence, however, internationally harmonised standards for the selection of specific drug combinations, dosing regimens, duration of supportive therapy and subsequent monitoring of fertility in treated bitches remain insufficiently established and require systematic synthesis.

The aim of this review was therefore to systematically synthesise and comparatively evaluate current evidence on the efficacy of different pharmacological protocols for the conservative treatment of canine pyometra, with particular emphasis on preservation of reproductive function, recurrence rates and the criteria required for their safe application in veterinary theriogenology.

Methodology of the systematic review. A systematic review of the scientific literature was conducted to examine conservative treatment of canine pyometra, the efficacy of individual therapeutic protocols, recurrence rates and post-treatment reproductive outcomes. Literature searching, screening, evaluation and analysis were performed using approaches consistent with those applied in systematic literature reviews.

Scientific publications were identified through Scopus, Web of Science, Google Scholar and the Ukrainian scientific periodicals database. Searches were conducted using keywords and combinations relevant to the scope of the review, including "canine pyometra", "bitch pyometra", "conservative treatment", "medical treatment", "aglepristone", "prostaglandin", "cloprostenol", "cabergoline", "reproductive outcome" and "fertility".

Publications evaluating aglepristone, prostaglandins and dopamine agonists, either alone or in combination, as well as adjunctive antimicrobial and supportive therapy, were considered for inclusion. Particular emphasis was placed on evidence relating to clinical efficacy, recovery, recurrence, treatment-related complications and restoration of reproductive function. The evidence base comprised clinical and retrospective studies, reviews and other relevant scientific publications included in the reference list of this review.

Following the initial search, the results were refined and publications were selected according to their relevance to the review question, scientific informativeness and availability of the required outcome data. Therapeutic protocols, drug dosages and administration regimens were compared alongside reported rates of clinical recovery, recurrence and subsequent pregnancy following conservative treatment. Particular attention was given to comparisons between monotherapy and combination protocols, especially regimens involving aglepristone, cloprostenol and cabergoline, as well as to the role of antimicrobial therapy and management of systemic disturbances associated with pyometra.

The findings were synthesised through qualitative comparative analysis of data reported in the selected publications, without conducting an original clinical experiment or quantitative meta-analysis. The resulting synthesis was used to characterise current evidence on the efficacy of conservative therapeutic protocols, recurrence rates and reproductive outcomes following medical treatment of canine pyometra.

Results and discussions. Numerous individual therapeutic approaches and protocols have been described in the available literature; however, the optimal treatment strategy should take into account the clinical form of the disease (open- or closed-cervix pyometra), the age and hormonal status of the animal, and the severity of endotoxaemia. Conservative management generally involves a combination of hormonal agents, including prostaglandins and antiprogestins, antimicrobial drugs, uterotonic and vitamin preparations, analgesics, antispasmodics, diuretics, hepatoprotective and immunostimulatory agents, together with measures aimed at correcting fluid and electrolyte disturbances, supporting vital organ function and promoting systemic detoxification (Feldman, 2000; Hall, 2012; Berezovskiy and Harenko, 2017; Prasad et al., 2017; Ziukina and Skliarov, 2019).

Rautela and Katiyar (2019) considered the inclusion of immunostimulatory agents with antioxidant activity appropriate in therapeutic protocols for bitches with pyometra and impaired immune function. The use of iodine-containing

preparations has also been described, with proposed effects on non-specific humoral immune mechanisms and redox processes, potentially contributing to systemic recovery and modulation of immune status (Khan et al., 2007; Shekhar, 2008; De Cramer, 2010; Sachan et al., 2019; Kumar and Pooja, 2023).

Another potentially promising approach involves the gonadotropin-releasing hormone antagonist acyline (Concannon, 2009; Batista et al., 2015; Kaçar, 2015; Kustritz, 2018). A single oral dose of acyline at 330 µg/kg combined with amoxicillin-clavulanate at 12.5 mg/kg orally twice daily for 7 days has shown promising therapeutic results (Batista et al., 2016).

Recent clinical evidence further supports the efficacy of aglepristone as a fertility-preserving treatment for canine pyometra. In a study involving 87 bitches, clinical recovery was achieved with aglepristone administered either as monotherapy or in combination with antimicrobial treatment. A shortened aglepristone regimen (10 mg/kg subcutaneously on days 0 and 1) was associated with a lower incidence of vaginal hyperplasia than a four-dose regimen (7% vs 53.3%), while maintaining clinical and reproductive efficacy; the overall pregnancy rate was 80% (Lopes et al., 2025).

Recurrence of pyometra remains possible following clinical recovery. Reported recurrence rates after aglepristone treatment range from 17.4% to 48.0%, whereas rates of 0–20% have been reported when aglepristone is combined with cloprostenol (Trasch et al., 2003; Fieni, 2006; Jurka et al., 2010; Contri et al., 2015; Ros et al., 2014; Gobello et al., 2003; Molina, 2015).

Adverse effects associated with aglepristone may include restlessness, depression, loss of appetite, polydipsia, diarrhoea, abdominal cramping, dyspnoea, decreased body temperature and local injection-site reactions (Fieni, 2006; Ros et al., 2014). Local pruritic reactions generally resolve within one week (Fieni, 2006; Pesch, 2017).

Aglepristone may also affect the interoestrous interval, with shortening reported in 19–43% of treated bitches (Trasch et al., 2003; Jurka et al., 2010; Contri et al., 2015). Trasch et al. (2003) followed treated bitches for 1 year and reported recurrence of pyometra during the subsequent oestrus in 18.9% of cases (Gobello et al., 2003; Jurka et al., 2010).

Gogny and Fiéni (2016) described a protocol in which aglepristone was administered subcutaneously at 10 mg/kg once daily on days 1, 2, 7 (or 8), 14 and, when clinical resolution had not been achieved, day 28. Reported success rates ranged from 46% to 100%, recurrence rates from 0% to 48%, and subsequent fertility rates from 69% to 85%.

The risk of severe adverse effects appears to be lower with aglepristone than with prostaglandins (Trasch et al., 2003; Gürbulak et al., 2005; Fieni, 2006; Jurka et al., 2010; Contri et al., 2015; Pesch, 2017). Several authors have reported successful treatment of canine pyometra with aglepristone without adverse effects (Hoffmann et al., 2000; Fieni et al., 2001; Gobello et al., 2003). In the study by Hagman (2018), aglepristone treatment resulted in clinical resolution in 9 of 10 animals, with no reported recurrence or adverse effects.

Thirumurugan and Rajasundaram (2011) compared three treatment protocols based on cloprostenol, aglepristone, or their combination. All three groups additionally received antimicrobial and fluid therapy. In bitches with open-cervix pyometra, all protocols achieved 100% treatment success. Aglepristone was nevertheless considered preferable because it required fewer administrations and was not associated with adverse effects.

More recent evidence indicates that aglepristone may achieve effective clinical resolution even without concomitant antimicrobial treatment, although vaginal hyperplasia may occur (Lopes et al., 2025). Unlike prostaglandins, aglepristone does not exert a direct luteolytic effect and is not associated with characteristic systemic adverse effects such as salivation, vomiting and diarrhoea (Fieni, 2006; Sethi et al., 2020).

Contri et al. (2015) proposed a modified aglepristone protocol comprising four subcutaneous injections at 10 mg/kg on days 1, 3, 6 and 9. All 47 bitches treated according to this regimen recovered, and no recurrence was recorded during the 24-month follow-up period (Contri et al., 2015; Hagman, 2018).

The comparative efficacy of different antiprogestin treatment regimens reported in clinical studies is summarised in Table 2.

Analysis of the data presented in Table 2 indicates that the conventional aglepristone protocol (10 mg/kg on days 1, 2 and 7–8) provides a high rate of initial clinical recovery (77.1–92.3%), although recurrence may occur in approximately 10–20% of cases during the subsequent 12 months (Hoffmann et al., 2000; Trasch et al., 2003; Fieni, 2006).

The highest efficacy was reported for the modified protocol proposed by Contri et al. (2015), in which aglepristone was administered at 10 mg/kg on days 1, 3, 6 and 9. Clinical recovery was achieved in 100% of treated bitches, with no recurrence recorded during the 24-month follow-up period (Contri et al., 2015).

Alizin has been used for the non-surgical treatment of canine pyometra. The clinical efficacy of aglepristone (Alizin) administered subcutaneously at 0.33 ml/kg on days 1, 2, 7 and 14, including its use in combination with intrauterine antimicrobial therapy selected on the basis of microbiological culture and antimicrobial susceptibility testing, has been supported by ultrasonographic, haematological and biochemical findings (Gürbulak et al., 2005).

Samoiliuk et al. (2018) reported successful treatment with Alizin in 100% of bitches with open-cervix pyometra. Despite the relatively high cost of the drug, this approach may be particularly valuable for reducing surgical risk and treating animals of breeding value.

Limitations of aglepristone treatment include the potential for allergic reactions associated with individual hypersensitivity, the risk of disease recurrence and the high cost of treatment, particularly in large dogs (Skliarov and Piatybrat, 2022).

Mifepristone administered at 2.5 mg/kg has demonstrated a high therapeutic efficacy of 83.33%; however, its clinical use is constrained by difficulties in accurate dosing across

Comparative efficacy of antiprogesterin treatment protocols in bitches with pyometra

Author / Study	Drug	Administration regimen and dosage	Clinical efficacy (%)	Recurrence rate (%)
Breitkopf et al. (1997)	Aglepristone	5–6 mg/kg subcutaneously on day 1 (two injections 24 h apart), and on days 3, 4, 8, 12 and 16	100	0
Hoffmann et al. (2000)	Aglepristone	10 mg/kg subcutaneously on days 1, 2 and 7	80.6–100	~18.9
Trasch et al. (2003)	Aglepristone	10 mg/kg subcutaneously on days 1, 2 and 7	92.3	9.8–18.9
Gurbulak et al. (2005)	Aglepristone	10 mg/kg subcutaneously on days 1, 2, 7 and 14	46	Not reported
Fieni (2006)	Aglepristone	10 mg/kg subcutaneously on days 1, 2 and 8 (and day 15 if required)	77.1	17.4–48
Contri et al. (2015)	Aglepristone	Modified protocol: 10 mg/kg subcutaneously on days 1, 3, 6 and 9	100	0 (during 24-month follow-up)
Urmila et al. (2022)	Mifepristone	2.5 mg/kg orally once daily for 5 days	83.3	Not reported

dogs of markedly different body sizes and by the lack of veterinary-specific formulations (Urmila et al., 2022). Combined administration of mifepristone and misoprostol may also have potential for the medical management of pyometra, particularly in bitches that develop pronounced adverse reactions to PGF_{2α} (Hiron et al., 2022).

Optimising the use of uterotonic agents (PGF_{2α} and its analogues). The use of uterotonic agents in the conservative management of canine pyometra is intended to stimulate myometrial contractility and accelerate evacuation of pathological contents from the uterine lumen (Henderson, 1984; Fieni et al., 2014; Melandri et al., 2019; Sethi et al., 2020; Hagman, 2023; Lopes et al., 2025). The principal drugs in this group are natural prostaglandin F_{2α} (dinoprost) and its synthetic analogues, particularly cloprostenol (Jackson, 1979; Swift et al., 1979; Nelson et al., 1982; Hagman et al., 2006; Lavin and Maki, 2023; Xavier et al., 2023; Kumar et al., 2024).

Prostaglandin monotherapy in bitches with pyometra has been associated with treatment success rates of 70–100% and subsequent fertility rates of 75–87% (Wallace and Casal, 2018).

Feldman and Nelson (2004) treated 103 bitches with open-cervix pyometra using natural prostaglandins and reported complete clinical recovery in 93% of cases. Approximately two-thirds of the animals recovered after an initial 5-day course, whereas the remainder required a second course of treatment. Administration of cloprostenol at 10 µg/kg for 5 days resulted in recovery in 75% of cases, with repeat treatment 10 days later increasing the success rate to 90% (Tainturier and Treboz, 1985). The therapeutic efficacy of PGF_{2α} is primarily attributable to its ability to induce uterine contractions. A luteolytic response has been reported in approximately 50% (Tainturier and Treboz, 1985) to 80% (Nudelmann, 1992) of treated bitches.

The synthetic prostaglandin analogue cloprostenol offers several potential advantages over natural prostaglandin (dinoprost), including greater selectivity for the myometrium, a longer duration of action and less pronounced systemic adverse effects (Patil et al., 2021; Xavier et al., 2023). A rational therapeutic strategy is to administer cloprostenol at the lowest effective dose following initial treatment with aglepristone. By antagonising progesterone-mediated

support and facilitating cervical opening, aglepristone creates more favourable conditions for subsequent uterine evacuation induced by cloprostenol (Contri et al., 2015; McCallin et al., 2022; Xavier et al., 2023; Abhay Kumar et al., 2025). This sequential approach may facilitate more rapid evacuation of purulent uterine contents.

At the same time, the use of either natural or synthetic prostaglandins as monotherapy has several important limitations:

- Risk of complications in closed-cervix pyometra. Administration of uterotonic agents in the absence of effective uterine drainage may increase intrauterine pressure, thereby increasing the risk of uterine rupture and subsequent peritonitis. Prostaglandin therapy should therefore be used with careful consideration of cervical patency and the overall clinical status of the animal (Fransson and Ragle, 2003; Lee et al., 2020; Xavier et al., 2023).

- Adverse effects. Natural prostaglandins may induce salivation, vomiting, diarrhoea, restlessness, tachycardia, tremors and abdominal pain. These systemic adverse reactions may limit their clinical use and necessitate careful monitoring of the animal throughout treatment (Fieni et al., 2014; Sethi et al., 2020).

- Need for repeated administration. The relatively short duration of action of natural PGF_{2α} necessitates repeated administration over several days, potentially reducing the practicality of the treatment protocol and increasing the burden on the animal.

- Dependence of efficacy on the clinical form of pyometra. Prostaglandins are generally more effective in open-cervix pyometra, in which drainage of pathological uterine contents can occur. In closed-cervix pyometra, uterotonic treatment requires particular caution because continued accumulation of uterine contents may increase intrauterine pressure.

- Limited efficacy of monotherapy. Prostaglandin administration without prior blockade of progesterone receptors may not consistently achieve sufficient cervical opening and complete evacuation of pathological uterine contents. Combining prostaglandins with antiprogesterins may therefore represent a more appropriate therapeutic strategy in carefully selected patients.

- **Recurrence.** Short- and long-term outcomes following PGF₂ α treatment of canine pyometra were evaluated by Meyers-Wallen et al. (1986). Dinoprost tromethamine was administered subcutaneously at 0.25 or 0.5 mg/kg body weight once daily for 3 days. During the first year after treatment, four bitches subsequently produced litters. Pyometra recurred in four bitches (40%) during this period, and these same animals experienced a further recurrence following repeat prostaglandin treatment. Three additional bitches developed recurrent pyometra 27 months after treatment, resulting in an overall recurrence rate of 77%. The authors suggested that subclinical disease might persist after treatment and subsequently become clinically apparent during diestrus. Despite the high recurrence rate, the approach was considered a practical treatment option for bitches with pyometra when preservation of reproductive function was desired.

- **Minimising adverse effects.** To reduce prostaglandin-associated adverse reactions, low-dose protocols with gradual dose escalation have been proposed (Arnold et al., 1988; Lange et al., 1997). Combination protocols in which prostaglandins are administered together with antiprogesterins have also been used to improve tolerability and therapeutic management (Contri et al., 2015; McCallin et al., 2023; Xavier et al., 2023; Abhay Kumar et al., 2025).

Very low doses of prostaglandins have been recommended to minimise treatment-related adverse effects, including cloprostenol at 1 μ g/kg subcutaneously from days 3 to 7 of treatment (Fieni et al., 2014). Sankhe et al. (2009) successfully treated bitches with open-cervix pyometra using low-dose prostaglandin therapy without reported adverse effects. For natural prostaglandins, doses of 10–50 μ g/kg administered three to five times daily for 3–7 days have been described (Kumari Baithalu et al., 2010). To improve tolerability, gradual dose escalation from a lower initial dose has been recommended (Wheaton and Barbee, 1993; Sachan et al., 2019).

For natural prostaglandin preparations, particularly dinoprost tromethamine (Sridevi et al., 2000; Pamdey et al., 2004), a dose of 0.1 mg/kg administered subcutaneously every 12–24 h until clinical recovery has been recommended in bitches. However, even this dose, which lies at the lower end of the recommended range, may be associated with undesirable adverse effects, contributing to increasing interest in alternative low-dose regimens and combination protocols (Hagman, 2018; Kutzler, 2019).

An alternative protocol involves an initial dose of 10 μ g/kg administered subcutaneously five times on the first day, followed by progressive escalation to 25 μ g/kg five times on the second day and 50 μ g/kg on the third day. Thereafter, 50 μ g/kg is administered three to five times daily from day 3 onwards for the remainder of the treatment period. Adverse effects were reported in 15% of treated bitches using this regimen (Verstegen, 2008; Hagman, 2018).

The absence of adverse effects following intravaginal administration of prostaglandin has also been reported by Gabor et al. (1999) and Urmila et al. (2022).

The efficacy of prostaglandins in the treatment of canine pyometra appears to depend more strongly on

uterine status than on the administered dose and has been associated more closely with repeated administration over 8–10 days than with the total cumulative dose. Comparison of the uterotonic effects of two intramuscular doses (250 μ g/kg versus 50 μ g/kg) in bitches during diestrus demonstrated comparable uterine contractions. The higher dose produced an effect lasting 32 ± 3 min, compared with 23 ± 3 min for the lower dose (Burke, 1982; Nelson et al., 1982).

The severity of prostaglandin-associated adverse effects may be reduced through measures aimed at limiting their systemic effects on smooth muscle (Tainturier and Treboz, 1985; Feldman and Nelson, 2004; Verstegen et al., 2008; Jena et al., 2013; Fieni et al., 2014; Greer, 2014; Hagman, 2018):

- prostaglandin doses may be progressively increased from the minimum therapeutic dose of 0.1 mg/kg to 0.25 mg/kg over 48–72 h;
- synthetic cloprostenol at 10 μ g/kg may be used instead of natural prostaglandins;
- pretreatment with atropine, prifinium or metopimazine may be administered 15 min before prostaglandin treatment;
- prostaglandins may be administered before feeding following a 4–6-h fasting period;
- affected dogs may be walked immediately after injection for approximately 15–20 min, with longer periods of 30–40 min used when appropriate.

In addition, to reduce the risk of serious adverse effects, prostaglandins are recommended primarily for younger bitches without hepatic, renal or cardiovascular disease (Metcalfe and Vischer, 2006).

The principal protocols for the use of uterotonic agents are compared in Table 3.

Analysis of the data presented in Table 3 indicates that the use of oxytocin in the treatment of pyometra is generally inappropriate, particularly in cases of closed-cervix pyometra. Although oxytocin stimulates myometrial contractions, it does not reliably promote cervical opening and may therefore increase intrauterine pressure, with a consequent risk of uterine rupture and peritonitis (Lavin and Maki, 2023; Xavier et al., 2023).

Dopamine agonists are a group of drugs with antiprolactin activity. From approximately day 25 after oestrus, they can exert an effective luteolytic action through suppression of prolactin and may be used in combination with prostaglandins to enhance the medical treatment of pyometra (England et al., 2007; Verstegen et al., 2008; Hagman, 2018). Dopamine agonists are ergot-derived compounds that act directly on D₂ dopamine receptors of lactotroph cells in the anterior pituitary, thereby suppressing prolactin (PRL) secretion. This reduction in PRL also suppresses milk production, making cabergoline a treatment of choice for pseudopregnancy in bitches (Gobello, 2006). Importantly, prolactin also acts as a major luteotrophic hormone regulating corpus luteum function during the second half of the canine luteal phase (Corrada et al., 2006).

The two principal dopamine agonists used in this context are cabergoline and bromocriptine. Cabergoline (Galastop) is generally preferred because it is associated with fewer adverse effects and requires less frequent administration

Dosage regimens and efficacy of uterotonic agents in bitches with pyometra

Drug	Dosage regimen and route of administration	Expected effect and recovery	Adverse effects
Dinoprost (<i>natural</i> PGF _{2α})	0.05–0.25 mg/kg subcutaneously 2–3 times daily for 5–7 days	Evacuation of uterine exudate; recovery rate 50–65%	Pronounced: vomiting, salivation, tachypnoea and restlessness
Cloprostenol (<i>synthetic</i> PGF _{2α})	1–2.5 µg/kg subcutaneously once daily or every other day (3–5 injections)	Pronounced uterotonic effect; recovery rate 60–75%	Mild to moderately pronounced systemic reactions
Cloprostenol (<i>low-dose protocol</i>)	1 µg/kg subcutaneously in combination with aglepristone (from day 3)	Accelerated uterine clearance; recovery rate 85–95%	Minimal and generally well tolerated
Oxytocin	0.5–1 IU/kg intramuscularly (older protocols)	Low efficacy (increases cervical tone only)	Low systemic toxicity, but a high risk of uterine rupture

than bromocriptine (Corrada et al., 2006; Verstegen et al., 2008). By suppressing PRL secretion and thereby reducing luteotrophic support of the corpus luteum, cabergoline can contribute to declining progesterone concentrations and may therefore be useful in the medical management of pyometra (Gobello, 2006). Because prolactin is required for luteal maintenance during canine pregnancy, repeated administration of cabergoline beyond approximately 25 days after ovulation results in a rapid decline in plasma progesterone concentrations and can subsequently induce termination of an unwanted pregnancy (Onclin et al., 1993).

Cabergoline is administered orally at 5 µg/kg once daily for 7 days, whereas bromocriptine is administered orally at 25 µg/kg three times daily for 7 days (Hagman, 2017). Cabergoline generally induces less vomiting than bromocriptine, representing an important advantage in clinical practice (Verstegen et al., 2008; Greer, 2014; Hagman, 2017; Greco and Davidson, 2017).

Dopamine agonists may be used either alone or in combination with prostaglandins (Verstegen et al., 2008; Hagman, 2017; Rautela and Katiyar, 2019).

Evaluation of synergistic combination protocols and their effects on fertility restoration. The contemporary development of conservative treatment for canine pyometra has been characterised by a shift from monotherapy towards combination pharmacological protocols integrating drugs with complementary mechanisms of action (Lee et al., 2020; Kumar et al., 2022; Krekeler and Hollinshead, 2023; Rocha et al., 2025; Abhay Kumar et al., 2025). Simultaneous or sequential targeting of different components of the disease pathogenesis, including progesterone receptor blockade, suppression of prolactin secretion and stimulation of myometrial contractility, represents a promising strategy for improving therapeutic efficacy and shortening the duration of conservative treatment (Singh et al., 2020; McCallin et al., 2022; Abhay Kumar et al., 2025; Rocha et al., 2025).

The most widely used combination pharmacotherapy approaches include:

- Aglepristone + cloprostenol: combining progesterone receptor blockade with prostaglandin-induced luteolysis and stimulation of myometrial contractility facilitates evacuation of pathological uterine contents (Kaya et al., 2014; Contri et al., 2015; Rocha et al., 2025).

- Aglepristone + cabergoline: combining antiprogesterin activity with suppression of prolactin secretion simultaneously targets different hormonal mechanisms involved in maintaining the pathological uterine environment (Corrada et al., 2006; England et al., 2007; Panasova and Vilialova, 2021).

- Combination protocol targeting three mechanisms of action: treatment with mifepristone, cabergoline and PGF_{2α} resulted in 100% clinical success and more rapid evacuation of uterine contents than the corresponding protocol without prostaglandin (Reddy et al., 2010; Sethi et al., 2020; Abhay Kumar et al., 2025).

A comparative analysis of clinical efficacy and subsequent fertility outcomes associated with different pharmacological approaches is presented in Table 4.

As shown in Table 4, the use of combination protocols increases clinical recovery rates to 90–100% and substantially reduces the risk of recurrence compared with monotherapy.

For breeding animals, the most important criterion of successful conservative treatment is preservation and restoration of reproductive capacity (Hagman, 2018; McCobb et al., 2022; Lopes et al., 2025). Current evidence indicates that reproductive performance can remain high following successful conservative treatment of pyometra. Lopes et al. (2025) reported a pregnancy rate of 80% following aglepristone treatment, whereas an earlier large-scale study using a combination of aglepristone and cloprostenol achieved pregnancy in 92.14% of treated bitches, most of which conceived during the first oestrus after treatment (Melandri et al., 2019; Sethi et al., 2020; Lopes et al., 2025).

Following successful conservative therapy, reversal of the progesterone-dependent uterine state and evacuation of pathological contents are accompanied by gradual regression of uterine abnormalities, which can be assessed through serial ultrasonographic monitoring (England, 2003; Fieni et al., 2014; Lee et al., 2020; Lopes et al., 2025; Rocha et al., 2025).

Rimer (1990) reported successful treatment of closed-cervix pyometra in a 15-month-old Bernese Mountain Dog using subcutaneous dinoprost tromethamine combined with co-trimoxazole. Dinoprost tromethamine was administered once daily at 0.25 mg/kg for 5 days, whereas co-trimoxazole was administered for one week. Prostaglandin-associated

**Comparative efficacy of combination treatment protocols and reproductive prognosis
in bitches following treatment for pyometra**

Treatment regimen / protocol	Clinical recovery (%)	Recurrence within 12–24 months (%)	Pregnancy at the first subsequent oestrus (%)	Sources
PGF ₂ α monotherapy (dinoprost/cloprostenol)	50–65	30–50	20–40	Ponomar'ova and Derkach (2012); Lavin and Maki (2023)
Aglepristone monotherapy (standard protocol)	77.1–92.3	10–20	60–70	Hoffmann et al. (2000); Trasch et al. (2003)
Aglepristone + cloprostenol (modified protocol)	90–95	5–10	75–85	Fieni et al. (2014); Contri et al. (2015)
Aglepristone + cabergoline	88–93	8–12	70–80	England et al. (2011); Panasova and Vilialova (2021)
Aglepristone + cloprostenol + cabergoline	95–100	0–5	80–90	Sethi et al. (2020); Krekeler and Hollinshead (2023)

adverse effects included hypersalivation and mild restlessness after each administration, together with vomiting approximately 20 min after the first two injections. Approximately one year later, the bitch was successfully bred.

Methylergometrine may also be used as a uterotonic agent. Its action on α -adrenergic receptors increases uterine tone and the frequency of uterine contractions. Kantharaj et al. (2018) included methylergometrine (0.125 mg) in a treatment protocol comprising ciprofloxacin (10 mg/kg twice daily) and fluid therapy for 7 days. The authors concluded that methylergometrine, when combined with antimicrobial and supportive fluid therapy, may be effective in the management of bitches with open-cervix pyometra.

Rationale for adjunctive antimicrobial, detoxification and pathogenetic therapy. Pharmacological management of canine pyometra cannot be restricted to hormonal or uterotonic agents alone, as comprehensive treatment must also address bacterial infection and, where required, provide appropriate supportive care (Fieni et al., 2014; McCobb et al., 2022; Xavier et al., 2023). In animals with pronounced endotoxaemia, a systemic inflammatory response and active microbial infection, the therapeutic protocol should therefore incorporate adjunctive measures aimed at controlling the infectious process and maintaining systemic physiological functions (Jitpean et al., 2014; Camozzi, 2020; Hagman, 2023; Xavier et al., 2023; Çolakoğlu and Karaca, 2025).

The main components of adjunctive pathogenetic and symptomatic therapy include:

- Rational antimicrobial therapy: systemic antimicrobial treatment should be selected according to disease severity, local patterns of antimicrobial resistance and, whenever possible, the results of bacterial culture and antimicrobial susceptibility testing. *E. coli* remains the most frequently isolated pathogen in canine pyometra; however, recent studies have demonstrated substantial variability in antimicrobial susceptibility profiles, limiting the appropriateness of empirical antimicrobial selection in the absence of microbiological testing (Fransson and Ragle, 2003; Ryzhykh et al., 2019; Bertero et al., 2024).

- Fluid and supportive therapy: in animals with systemic disturbances, fluid therapy is directed towards restoring adequate tissue perfusion, correcting dehydration

and electrolyte imbalances, and supporting organ function, particularly in the presence of sepsis or organ dysfunction (Lavin and Maki, 2023; Çolakoğlu and Karaca, 2025).

- Pathogenetic and symptomatic support: depending on the clinical status of the patient, supportive management may include analgesia, correction of metabolic disturbances and other intensive-care measures. Treatment should be individualised according to the clinical condition of the animal and the assessed risk of organ dysfunction (Sethi et al., 2020; Xavier et al., 2023; Bertero et al., 2024; Çolakoğlu and Karaca, 2025).

The principal adjunctive pharmacological interventions and the rationale for their use are summarised in Table 5.

As indicated by the data presented in Table 5, antimicrobial therapy should be continued for at least 10–14 days and for a minimum of 3–5 days after complete cessation of uterine discharge and normalisation of the ultrasonographic findings (Fieni et al., 2014; Krekeler and Hollinshead, 2023). Inappropriate antimicrobial use or premature discontinuation of treatment may contribute to persistence of the infectious process and the development of antimicrobial resistance, thereby complicating subsequent treatment of pyometra (Hagman, 2005; Bertero et al., 2024; Camozzi et al., 2020, 2026).

Current evidence also highlights the importance of therapeutic measures aimed at limiting endotoxaemia associated with bacterial infection. Release of bacterial endotoxins into the circulation may contribute substantially to systemic complications and aggravate the clinical course of the disease (Demirel and Küplülü, 2010). Septicaemia has been reported in 15% of affected bitches (Feldman and Nelson, 2004), making systemic antimicrobial therapy an important component of conservative management. Its effectiveness, however, depends substantially on the antimicrobial resistance profile of the causative microorganisms (Hagman et al., 2005; Harada et al., 2012; Muzyka et al., 2012; Yoon et al., 2017; Hagman, 2018).

Antimicrobial therapy serves two principal purposes: first, to control bacterial infection within the uterus and, second, to reduce the risk of systemic dissemination of microorganisms through the bloodstream (Wiebe and Howard, 2009; Melandri et al., 2019).

Adjunctive multimodal therapy during conservative treatment of pyometra in bitches

Drug group	Representative agent / Pharmacological formulation	Dosage and route of administration	Therapeutic purpose and effect
Broad-spectrum antibiotics	Amoxicillin + clavulanate (<i>Synulox</i>)	12.5–25 mg/kg subcutaneously or orally twice daily for 10–14 days	Elimination of <i>E. coli</i> and associated bacterial flora
Fluoroquinolones	Enrofloxacin / marbofloxacin	5 mg/kg subcutaneously or orally once daily for 7–10 days	Suppression of Gram-negative bacterial flora
Fluid therapy	Ringer's solution, Sterofundin	20–40 ml/kg/day by intravenous infusion for 3–5 days	Correction of dehydration and electrolyte disturbances; systemic supportive therapy
NSAIDs	Meloxicam	0.1–0.2 mg/kg subcutaneously or orally once daily for 3–5 days	Analgesic, antipyretic and anti-inflammatory effects
Pathogenetic therapy	0.5% procaine solution	Lumbar blockade according to V. V. Mosin, 1 ml/kg	Relief of visceral spasm and improvement of tissue trophism

Selection of an antimicrobial agent should take into account the susceptibility of microorganisms associated with pyometra (Hall, 2012). Evidence from previous studies indicates that many pathogenic bacterial isolates recovered from the uterus of bitches with pyometra are susceptible to amoxicillin–clavulanate, fluoroquinolones, including norfloxacin, enrofloxacin and ciprofloxacin, and third-generation cephalosporins such as cefotaxime (Coggan et al., 2008; Sant'Anna et al., 2014; Robaj et al., 2018).

Ideally, bacterial culture and antimicrobial susceptibility testing should be performed before empirical antimicrobial therapy is initiated. However, because pyometra is potentially life-threatening, empirical antimicrobial treatment may need to be initiated at the time of diagnosis rather than delayed until microbiological results become available, with subsequent adjustment of therapy according to culture and susceptibility findings where appropriate (Wiebe and Howard, 2009).

According to Robaj et al. (2018), more than 30% of all bacterial isolates, including *E. coli*, *Staphylococcus intermedius*, *Streptococcus pyogenes* and *Pseudomonas aeruginosa* ($n = 52$), were susceptible to tetracycline, ampicillin, gentamicin, penicillin G and lincomycin, whereas *E. coli* showed the highest resistance to penicillin G (67.9%). These findings were broadly consistent with those reported in earlier studies (Bartoskova et al., 2007; Verstegen et al., 2008).

Resistance to ampicillin and penicillin may be associated with the frequent use of these antimicrobials in veterinary practice for the treatment of severe infections in dogs. Bacteria involved in persistent infections, including pyometra, may carry resistance plasmids, further complicating control of the infectious process (Chang et al., 2014). Screening for antimicrobial resistance among isolates of *E. coli*, *Staphylococcus intermedius* and *Streptococcus pyogenes* is therefore warranted.

Antimicrobial therapy for canine pyometra is generally directed primarily against *E. coli*. Initial antimicrobial options include ampicillin (10–20 mg/kg), amoxicillin–clavulanic acid (10–20 mg/kg) or second-generation cephalosporins, particularly cefoxitin (10–30 mg/kg intravenously) (Roberts et al., 2003). When bacterial culture identifies *Proteus* spp.,

ciprofloxacin or streptomycin may be considered according to antimicrobial susceptibility findings (Ukwueze and Orajaka, 2014).

The combination of enrofloxacin and amoxicillin–clavulanate broadens the spectrum of antimicrobial activity and may reduce persistence of bacteria resistant to either agent alone (Gobello et al., 2003; Hagman and Greko, 2005; Fieni, 2006; Wiebe and Howard, 2009; Fieni et al., 2014; Contri et al., 2015). Fluoroquinolones, particularly enrofloxacin, also achieve substantial concentrations in the canine myometrium, with concentrations in uterine fluid potentially exceeding those measured in plasma (Brown, 1996).

Current guidelines for antimicrobial use in companion animals identify fluoroquinolones such as enrofloxacin and amoxicillin–clavulanate as therapeutic options for pyometra, although their relative positioning within treatment recommendations differs (Xavier et al., 2023). Finnish and Swedish guidelines, for example, favour sulfadoxine–trimethoprim and ampicillin (Elfing et al., 2016; Turkki et al., 2023). Studies conducted in different countries indicate that many of the antimicrobials recommended for pyometra retain activity against bacterial isolates obtained from affected dogs. Other agents reported to be effective include cephalothin, streptomycin and gentamicin (Hagman and Greko, 2005; Inoue et al., 2013; Agostinho et al., 2014; Rocha et al., 2021; Lansubakul et al., 2022).

A recent retrospective analysis further supported the use of ampicillin or amoxicillin when antimicrobial therapy is indicated, particularly in bitches presenting with moderate to severe systemic depression (Turkki et al., 2023). Clinical studies have also reported favourable outcomes with cephalosporins, potentiated sulphonamides and amoxicillin, either alone or combined with clavulanic acid (Verstegen et al., 2008; Bassessar et al., 2013; Gupta et al., 2013; Bagri et al., 2022).

Based on evidence that cephalosporins retain antimicrobial activity against microorganisms associated with infectious diseases in companion animals (Muzyka et al., 2012), the therapeutic efficacy of cefazolin has also been investigated. The treatment regimen included oxytocin, PGF_{2α} (Enzaprost, Estrofan), vitamin C and

cefazolin. Cefazolin showed high antibacterial activity against *Staphylococcus aureus*, *Escherichia coli* and *Streptococcus pyogenes* isolates recovered from affected animals. The authors therefore considered cefazolin an effective antimicrobial agent for infections of the female reproductive tract caused by susceptible microorganisms.

A range of other antimicrobial agents and combinations has also been incorporated into treatment protocols. For example, cefotaxime (50 mg/kg) combined with metronidazole (20 mg/kg) has been administered for 10 days. Harenko et al. (2003) reported the use of 14 broad-spectrum antimicrobials, including ceftriaxone at 10–20 mg/kg intramuscularly for 5–7 days and oral Synulox at 12.5 mg/kg for 3 weeks.

More recent data describe the use of 16 different antimicrobials, of which amoxicillin/clavulanate potassium (86%), enrofloxacin (52%), cefazolin (37%) and ampicillin/sulbactam (22%) were the most frequently administered.

Contrary to the original hypothesis, Demirel and Küplülü (2010) reported better treatment outcomes with ampicillin alone than with the combination of polymyxin E and ampicillin.

Antimicrobial therapy has also been combined with intrauterine administration of foaming preparations. Because recurrence remains possible, continued clinical monitoring after the subsequent oestrus has been recommended (Antonov et al., 2015). Intrauterine antimicrobial administration and irrigation with povidone–iodine have likewise been used in bitches with open-cervix pyometra (Sen et al., 2001; De Cramer, 2010).

Recent studies and consensus statements in veterinary and human medicine increasingly emphasise the need for more judicious antimicrobial use (Lavin and Maki, 2023). Antimicrobial administration contributes to the selection and dissemination of antimicrobial-resistant microorganisms in the environment, potentially compromising the subsequent treatment of bacterial infections (Inoue et al., 2013; Agostinho et al., 2014; Guardabassi et al., 2018; Robaj et al., 2018; Weese et al., 2015, 2021; Rocha et al., 2022). Given the limitations of antimicrobial monotherapy and the considerable adaptive capacity of bacterial populations, prolonged use of the same antimicrobial agent should be avoided where possible to reduce selective pressure for resistance. The American College of Veterinary Internal Medicine recommends antimicrobial stewardship strategies that favour narrow-spectrum agents where appropriate and avoidance of antimicrobial treatment when effective alternatives are available (Morley et al., 2005; Weese et al., 2015).

In rare cases, pyometra may be complicated by fungal infection, including infection with *Candida* spp. (Han et al., 2011). However, evidence supporting specific antifungal treatment strategies for fungal complications of canine pyometra remains limited.

Natural or synthetic prostaglandins administered in combination with antimicrobial therapy have been reported to achieve successful treatment of open-cervix pyometra, with some studies reporting success rates of up to 100% (Valocky et al., 1997).

Gilbert et al. (1989) retrospectively evaluated 40 cases of canine pyometritis treated with prostaglandins and broad-spectrum antimicrobial agents. Treatment involved dinoprost, the tromethamine salt of PGF₂α (PGF₂α-THAM), or luproliol, a synthetic prostaglandin analogue, together with broad-spectrum antimicrobials. Prostaglandin treatment lasted from 2 to 26 days, with doses ranging from 26.8 to 258 µg/kg. Clinical recovery was achieved in 33 of the 40 bitches. Of the 14 bitches subsequently intended for breeding, nine eventually produced litters. Long-term complications included anoestrus, recurrent metritis, failure to conceive and abortion. One or more of these complications occurred in nine of the 20 bitches for which long-term follow-up information was available.

To evaluate the efficacy of different treatment strategies, Khan et al. (2007) compared several protocols combining prostaglandins with antimicrobial therapy. Bitches in group 1 received cloprostenol plus intramuscular antimicrobials, resulting in a treatment success rate of 83.33%. Group 2 received cloprostenol plus intrauterine antimicrobials, with the same success rate of 83.33%. Group 3 received cloprostenol combined with an intramuscular antimicrobial and intrauterine povidone–iodine, achieving a treatment success rate of 100%. By contrast, group 4 received intramuscular antimicrobials plus intrauterine povidone–iodine without cloprostenol, resulting in a success rate of 66.66%.

Kostyshyn et al. (2022) evaluated the antimicrobial preparations Amoksidev 15 and Enroxil 5% as components of multimodal treatment regimens that also included Dinolytic (Enzaprost-F), No-Spa, Devivit Complex, Tioprotectin 2.5% and herbal decoctions of nettle, raspberry, chamomile and *Orthilia secunda* ('boar's uterus'). Conservative treatment incorporating Amoksidev 15 resulted in clinical recovery in 70% of affected bitches. This multimodal regimen was also associated with a more rapid return of physiological variables towards reference values than the comparator regimen containing Enroxil 5%.

The conservative treatment protocol evaluated by Samoilenko and Ivashenko (2021) combined PGF₂α to facilitate rapid evacuation of pathological uterine exudate with the antimicrobial agent Ciprolet, the general supportive preparation Catosal and Rheopolyglucin solution. The study included 14 bitches of different breeds and ages, seven with open-cervix and seven with closed-cervix pyometra. Among bitches with open-cervix pyometra, three of seven (42.8%) recovered following conservative treatment; however, two of these three animals (66.6%) subsequently experienced recurrence. Among bitches with closed-cervix pyometra, two of seven (28.6%) recovered, but both developed recurrent disease within 6 months.

Shvets and Ivashenko (2018) evaluated a treatment protocol based on agents inducing myometrial contractions and luteolysis (prostaglandin), a metabolic stimulant (Catosal), a plasma-substituting solution (Haemodes) and the first-generation cephalosporin cefazolin. Of the eight bitches subjected to conservative treatment, only one achieved clinical recovery accompanied by restoration of the normal morphofunctional state of the uterus. In

all remaining animals, recurrence was observed, with persistent discharge of varying amounts of exudate despite an apparent improvement in their general clinical condition. To prevent recurrent pyometra and chronic intoxication, these animals subsequently underwent hysterectomy and ovariectomy.

Shah et al. (2016) investigated prostaglandin therapy administered either alone or in combination with mifepristone. In group 1, dinoprost tromethamine (natural PGF₂α) was administered subcutaneously at progressively increasing doses of 50–200 µg/kg from days 1 to 5 (day 1, 50 µg/kg; day 2, 100 µg/kg; day 3, 150 µg/kg; and days 4 and 5, 200 µg/kg). In group 2, mifepristone was administered orally at 2.5 mg/kg on days 1, 2 and 8, together with dinoprost tromethamine given subcutaneously at progressively increasing doses of 50–200 µg/kg from days 3 to 7. Concurrent antimicrobial treatment comprised enrofloxacin (5 mg/kg for 5–7 days) combined with either amoxicillin–dicloxacillin or amoxicillin–clavulanate (14 mg/kg body weight for 7–30 days). Supportive treatment, including intravenous fluids and multivitamins, was provided when required. Eleven of the 12 animals recovered following treatment, and recurrence before the subsequent oestrous cycle was observed in only one case. Clinical signs, uterine diameter and haematological and biochemical variables had returned to normal by day 14 after treatment initiation in both groups. On day 7, plasma progesterone concentrations decreased in the PGF₂α-only group but increased in the group receiving the antiprogesterin–PGF₂α combination. The authors concluded that mifepristone represents a safe and promising option for facilitating cervical opening in bitches with closed-cervix pyometra.

Although treatment success rates approaching 100% have been reported with PGF₂α in selected studies, such findings should be interpreted in the context of patient selection, disease severity and the specific treatment protocol used.

Vasylets and Plakhotniuk (2021) found the lowest therapeutic efficacy in the control group, in which bitches were treated with Ringer–Locke solution, Cobactan, Dinolytic and Dexafort. Clinical signs had resolved in 33.3% of animals by day 4, and overall therapeutic efficacy reached 55.5% by day 5. In one bitch (11.1%), clinical signs did not resolve completely, with persistent discharge of white purulent exudate; pyometra was subsequently diagnosed in this animal. Addition of the immunostimulatory agent Roncoleukin to the same basic regimen in the first experimental group improved treatment efficacy. Signs of metritis had resolved in 11.1% of bitches by day 3, in a further 44.4% by day 4 and in 33.4% by day 5, whereas signs of uterine inflammation disappeared in the remaining animal by day 7. The greatest efficacy was achieved when the antiprogesterin aglepristone (Alizin) was added to the basic treatment regimen in the second experimental group. Clinical signs of uterine inflammation had resolved in 22.2% of bitches by the end of day 3 and in a further 44.4% by day 4, with clinical recovery observed in all animals by the end of day 5.

Voskoboinyk and Plakhotniuk (2020) evaluated a medical protocol comprising subcutaneous aglepristone

(10 mg/kg body weight every 24 h on days 1, 3, 6 and 9) and Synulox (8.75 mg/kg body weight every 24 h for 14 days), together with two days of fluid therapy consisting of 200 ml Ringer's lactate and 100 ml balanced glucose solution. Compared with the control group treated surgically, the proportion of animals achieving recovery after medical treatment was 25.0 percentage points lower, whereas the proportion experiencing disease recurrence was 25.0 percentage points higher. Nevertheless, conservative treatment preserved reproductive potential, with 50.0% of treated bitches subsequently producing offspring.

Dadona et al. (2023) described treatment based on aglepristone (Alizin®, Virbac) combined with antimicrobial and anti-inflammatory treatment, analgesia and gastroprotective therapy, resulting in clinical recovery. Three years later, the bitch underwent artificial insemination, after which an uncomplicated pregnancy was confirmed and two puppies were delivered. The treatment was therefore considered successful in achieving clinical recovery, complete uterine involution and restoration of reproductive function.

Recent reviews (Xavier et al., 2023, 2024) reinforce the conclusion that no universally accepted protocol for conservative treatment has yet been established. Nevertheless, combination regimens integrating antiprogesterin, dopaminergic and prostaglandin-mediated mechanisms, including aglepristone, cabergoline and prostaglandins, appear among the most promising strategies for improving clinical efficacy while limiting recurrence.

Taken together, supportive fluid and detoxification therapy and appropriately selected antimicrobial treatment represent important components of multimodal conservative management, particularly during the initial stages of disease. By stabilising the patient, controlling bacterial infection and correcting systemic disturbances, these measures provide the clinical conditions required for antiprogesterins and uterotonic agents to exert their intended therapeutic effects.

Conclusions:

1. Aglepristone is an effective component of conservative treatment for canine pyometra. With the standard protocol, primary clinical recovery rates ranged from 77.1% to 92.3%, whereas the modified protocol of 10 mg/kg administered on days 1, 3, 6 and 9 achieved 100% clinical recovery in the cited study, with no recurrence during the 24-month follow-up period.

2. Prostaglandins stimulate myometrial contractions and facilitate evacuation of uterine contents, although their efficacy depends on the condition of the uterus and the possibility of adequate uterine drainage. Their administration may be associated with systemic adverse effects and requires particular caution in closed-cervix pyometra because of the risk of increased intrauterine pressure, uterine rupture and peritonitis.

3. Combination pharmacological protocols involving antiprogesterins, prostaglandins and dopamine agonists showed higher clinical efficacy and lower recurrence rates than the monotherapy protocols reviewed. Reported clinical recovery rates were 90–95% for aglepristone + cloprostenol, 88–93% for aglepristone + cabergoline and 95–100% for aglepristone + cloprostenol + cabergoline.

4. Reproductive function can be restored following successful conservative treatment. Reported pregnancy rates reached 80% following aglepristone treatment and 92.14% following combined aglepristone and cloprostenol treatment. Nevertheless, recurrence of pyometra and reproductive complications have been reported after treatment and should be considered when assessing the long-term prognosis.

5. Conservative pharmacological management may require concurrent antimicrobial, fluid, detoxification and other supportive treatment according to the clinical

condition of the animal. Selection of antimicrobial agents should take into account the susceptibility of the causative microorganisms and, whenever feasible, should be guided by bacterial culture and antimicrobial susceptibility testing.

6. The evidence reviewed does not support a single universally applicable standardised protocol for the conservative treatment of canine pyometra. Rather, the available findings support an individualised selection of the therapeutic regimen according to the clinical circumstances, accompanied by continued monitoring of the patient's clinical status and ultrasonographic assessment of uterine involution.

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Склярів П. М., доктор ветеринарних наук, професор, Дніпровський державний аграрно-економічний університет, м. Дніпро, Україна

Вакулик В. В., кандидат історичних наук, доцент, Дніпровський державний аграрно-економічний університет, м. Дніпро, Україна

Білий Д. Д., доктор ветеринарних наук, професор, Дніпровський державний аграрно-економічний університет, м. Дніпро, Україна

Милостивий Р. В., кандидат ветеринарних наук, доцент, Дніпровський державний аграрно-економічний університет, м. Дніпро, Україна

Чекан О. М., доктор ветеринарних наук, професор, Сумський національний аграрний університет, м. Суми, Україна

Консервативне лікування піометри у собак. Частина II: терапевтичні протоколи, клінічна ефективність та репродуктивні результати

У статті систематизовано та проаналізовано дані наукової літератури щодо сучасних протоколів консервативного лікування піометри у сук, їх клінічної ефективності, частоти рецидивів та відновлення репродуктивної функції. Особливу увагу приділено застосуванню антипрогестинів, простагландинів, агоністів дофаміну та їх комбінованих схем, а також супутній антибактеріальній, інфузійній і патогенетичній терапії.

Консервативне лікування не є універсальним методом і потребує диференційного відбору пацієнтів. Воно протипоказане при тяжкому сепсисі, розриві матки, перитоніті та тяжкій нирковій або печінковій недостатності. Aglepristone продемонстрував високу клінічну ефективність: за класичними протоколами первинне одужання становило 77,1–92,3%, а за модифікованої схеми з введенням 10 мг/кг на 1, 3, 6 і 9-ту добу – 100% без зареєстрованих рецидивів протягом 24 місяців. Ефективність простагландинів при монотерапії становила 70–100%, однак їх застосування супроводжується ризиком системних побічних реакцій і потребує особливої обережності при закритій формі піометри. Комбінування aglepristone з cloprostenol підвищувало клінічну ефективність до 90–95%,

а додавання cabergoline – до 95–100%, при цьому частота рецидивів знижувалася до 0–5%. Після успішного консервативного лікування відновлення репродуктивної функції було продемонстровано в різних дослідженнях: рівень вагітності після застосування aglepristone становив 80%, а при його комбінації з cloprostenol – 92,14%. Ефективність терапії також залежить від адекватного контролю бактеріальної інфекції, ендотоксикозу, водно-електролітних порушень та системних розладів. Ультрасонографічний моніторинг дає змогу контролювати регрес патологічних змін матки після лікування.

Сучасні дані свідчать про високу ефективність комбінованих фармакологічних протоколів порівняно з монотерапією, однак універсального стандартизованого протоколу консервативного лікування піометри у сук досі не сформульовано.

Ключові слова: піометра, суки, консервативне лікування, aglepristone, prostaglandins, cloprostenol, cabergoline, репродуктивна функція, рецидив.

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