

REVIEW ARTICLE

Ovarian pain in the mare: Clinical implications of mittelschmerz and oestrus-related behavioural abnormalities

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Summary

Mittelschmerz is a well-recognised benign peri-ovulatory pain syndrome in women and, by physiological analogy, may also occur in mares. In equine practice, peri-ovulatory ovarian pain has been associated with transient discomfort, colic-like signs and behavioural changes, although its true clinical relevance remains poorly defined. This narrative mini-review summarises current knowledge on the pathophysiology, clinical presentation, diagnostic challenges and management of ovarian pain in mares, integrating evidence from equine studies with established concepts derived from human medicine. In women, mittelschmerz is temporally associated with the luteinising hormone surge and prostaglandin-mediated ovarian smooth muscle contractions. Similar mechanisms have been proposed in mares, in which peri-ovulatory ovarian sensitivity may be detected during clinical examination but cannot be reliably used to predict ovulation. Behavioural abnormalities observed during oestrus are frequently attributed to ovarian activity or sex-steroid fluctuations; however, nonreproductive causes must be carefully excluded. In addition to physiological ovarian activity, both non-neoplastic and neoplastic ovarian disorders may induce chronic discomfort and behavioural alterations in mares, often posing diagnostic challenges due to overlapping ultrasonographic features with normal preovulatory follicles. Therapeutic strategies include hormonal suppression, induction of pseudopregnancy, immunisation against gonadotropin-releasing hormone and surgical intervention. While ovariectomy effectively resolves ovarian pain, its efficacy in correcting altered behaviour is variable. A multimodal diagnostic approach is essential to distinguish physiological ovarian pain from pathological conditions and behavioural disorders, thereby supporting appropriate clinical decision-making in equine practice.

KEYWORDS

horse, mare, mittelschmerz, oestrus behaviour, ovarian pain, ovariectomy

INTRODUCTION

Ovarian activity in the mare is closely associated with a range of physiological and behavioural changes, particularly during the peri-ovulatory period. While oestrus-related behavioural alterations are widely recognised in equine practice, the potential contribution of

ovarian pain to these manifestations remains poorly defined and often underestimated. In clinical settings, mares presenting with discomfort, reduced performance or undesirable behaviour are frequently assumed to be exhibiting normal oestrus-related responses, although underlying nociceptive mechanisms may play a role.

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In women, mittelschmerz is a well-described benign peri-ovulatory pain syndrome associated with the luteinising hormone surge and prostaglandin-mediated follicular events. Despite clear physiological similarities between species, the concept of mittelschmerz has received limited attention in the mare, and its clinical relevance remains unclear.

Furthermore, distinguishing physiological ovarian pain from pathological conditions, such as ovarian neoplasia, haemorrhagic an-ovulatory follicles or inflammatory processes, remains challenging. Overlapping clinical signs and ultrasonographic findings may complicate decision-making and increase the risk of inappropriate or unnecessary interventions. In addition, the relationship between ovarian pain and oestrus-related behavioural abnormalities remains controversial, with limited consensus on appropriate management strategies.

The objective of this narrative review is to synthesise current knowledge on ovarian pain in the mare, integrating evidence from equine literature with established concepts derived from human medicine. Specifically, this review aims to (i) describe the proposed pathophysiological mechanisms underlying peri-ovulatory pain, (ii) examine its clinical presentation and diagnostic challenges, (iii) differentiate physiological from pathological causes of ovarian discomfort and (iv) evaluate current therapeutic approaches and their implications for clinical practice. By providing a comparative and clinically oriented perspective, this review seeks to improve recognition of ovarian pain in mares and support more informed diagnostic and therapeutic decision-making.

MITTELSCHMERZ

In women, mittelschmerz refers to a transient lower abdominal pain occurring around the peri-ovulatory phase of the menstrual cycle. This condition is generally regarded as benign and is reported by a substantial proportion of women of reproductive age, with some individuals experiencing recurrent episodes across multiple cycles. The symptom typically develops only after ovulatory cycles have become established and is therefore uncommon in the early post-menarche years. Its occurrence may be intermittent, and affected women do not always associate the pain with the ovulatory process (Marinho et al., 1982).

Clinical presentation ranges from mild discomfort to intense, sometimes incapacitating pain. The sensation is usually unilateral and reflects the ovary undergoing dominant follicular development, resulting in pain localised to either iliac fossa, depending on the cycle (Marinho et al., 1982). Because the onset of pain often coincides with ovulation, mittelschmerz has been proposed as a potential clinical indicator of the fertile window within the menstrual cycle (O'Herlihy et al., 1980). In most cases, symptoms resolve spontaneously within several hours; however, prolonged pain lasting until the onset of menstruation has been described, particularly in women with a history of ovarian surgery (cystectomy, aspiration). Additional accompanying symptoms, such as mild lower back pain, may also occur (Charlewood, 1958).

From a diagnostic perspective, mittelschmerz may resemble a range of gynaecological disorders as well as acute abdominal conditions, including appendicitis, thereby increasing the risk of misdiagnosis and unnecessary surgical intervention. Overlapping clinical features – such as abdominal tenderness, guarding, leucocytosis and fever – can complicate differential diagnosis. Consequently, when assessing acute lower abdominal pain in women of reproductive age, clinicians should systematically consider gynaecological aetiologies as part of the diagnostic work-up (Hatipoglu et al., 2014). Understanding the mechanisms of mittelschmerz in women provides a useful physiological framework for interpreting peri-ovulatory ovarian pain in mares.

OVARIAN PAIN (MITTELSCHMERZ) IN THE MARE

Mares may experience ovarian pain associated with ovulation (McKinnon, 1998). Additional signs, including changes in follicle shape, uterine oedema and cervical relaxation, often accompany this tenderness. At this stage, mares typically turn their heads, but they may also kick, lie down or attempt to avoid manipulation. Colic-like symptoms linked to ovulation have also been reported (Cox & DeBowes, 1987).

In some mares, ovarian sensitivity during transrectal palpation may be evident within 12 h before ovulation, although certain individuals exhibit consistent sensitivity regardless of the cycle phase. Discomfort is more commonly observed when the site of recent ovulation is palpated, and ultrasonography is frequently used to achieve a definitive diagnosis (McKinnon, 1998). For this reason, expressions of pain or discomfort during transrectal ovarian palpation cannot be considered a reliable predictor of imminent ovulation.

OESTRUS BEHAVIOURAL ABNORMALITIES IN THE MARE

During oestrus, working equids often display fewer cooperative behaviours, and in some cases progress to overtly aggressive behaviours (Jorgensen et al., 1996; Kamm & Hendrickson, 2007; Petrizzi et al., 2020; Straticò et al., 2023). In clinical practice, veterinarians are frequently presented with mares described as behaving 'badly', either persistently or at regular or irregular intervals. Owners or riders commonly attribute these behaviours to the mare being in oestrus or to fluctuations in reproductive hormones. However, abnormal behaviour is not consistently associated with identifiable hormonal alterations. A retrospective study by Huggins et al. reported that behavioural abnormalities in mares were rarely correlated with changes in hormonal markers of granulosa cell tumours, highlighting the complexity of attributing behavioural signs solely to ovarian dysfunction (Huggins et al., 2024). A survey by the American Association of Equine Practitioners reported that 90% of respondents believed oestrus had a significant negative impact on their mares' athletic performance, whereas only 1% perceived no meaningful effect (Jorgensen et al., 1996).

Undesirable behaviours observed in mares are varied and may include an unwillingness to respond to rider cues, reluctance to engage the hindlimbs, poor behaviour under saddle, bucking, rearing, overt reproductive behaviours (such as tail swishing, squealing and clitoral eversion), as well as aggression or even stallion-like behaviour towards other horses or people (Crabtree, 2011; Heaton et al., 2018; Hedberg et al., 2007; Jorgensen et al., 1996; McCue, 2003). The oestrous cycle also appears to influence molting, leading to frequent urination, mouthing, excessive tail swishing, reduced working performance and unwillingness to work (Heaton et al., 2018; Petrizzi et al., 2020).

It is assumed that, when evaluating such problems, the clinician has ruled out nonreproductive causes – such as musculoskeletal, soft-tissue, gastric or dental pain – and verified a temporal association between the behaviour and the oestrous cycle or ovarian discomfort. Elevated oestrogen levels may exert direct or indirect effects on behaviour, and abdominal discomfort may further contribute. These behavioural changes during oestrus can significantly affect a mare's trainability and athletic performance, underscoring the need for a deeper understanding of the physiological mechanisms involved and for potential interventions to mitigate these effects.

OTHER CAUSES OF OVARIAN PAIN IN THE MARE

In addition to physiological ovarian activity and peri-ovulatory discomfort, several pathological ovarian conditions may also contribute to chronic pain and behavioural abnormalities in mares. These include non-neoplastic (abscesses, haematomas, haemorrhagic anovulatory follicles) (Carluccio et al., 2020; Curtin, 2003; Ramirez et al., 1999) and neoplastic conditions (granulosa theca cell tumours, teratomas or cystadenomas) (Card, 2011; Straticò et al., 2023). In non-neoplastic conditions, abdominal discomfort due to ovarian enlargement and inflammation is the cause of the abnormal behaviour, whereas in neoplasia, there could be an additional hormonal issue.

Differential diagnosis is further complicated by the fact that many of these conditions share similar ultrasonographic characteristics with preovulatory follicles. This diagnostic complexity is well recognised, particularly in the context of granulosa cell tumours and other ovarian conditions, where overlapping clinical, ultrasonographic and endocrine features may hinder definitive diagnosis (Renaudin et al., 2021). A multimodal approach is necessary, integrating hormonal assays with imaging techniques to precisely identify the underlying pathology and guide appropriate therapeutic strategies (Korany et al., 2020).

OVARIAN PAIN (MITTELSCHMERZ) THERAPEUTIC STRATEGIES

Once physiological and pathological causes of ovarian pain have been considered, several therapeutic strategies can be employed

to alleviate discomfort and manage associated behavioural abnormalities. Mittelschmerz has been shown to occur in temporal association with the peri-ovulatory surge in circulating luteinising hormone (LH), coinciding with the phase of rapid follicular growth. Current evidence suggests that the pain is not primarily caused by mechanical stretching of the follicular wall. Instead, the LH surge appears to enhance contractile activity of the ovarian perifollicular smooth muscle through prostaglandin-dependent mechanisms, which may account for the painful sensation experienced during this period (Durai & Ng, 2009; O'Herlihy et al., 1980; Won & Abbott, 2010).

Elevated concentrations of prostaglandin E2 (PGE2) are essential for normal ovulation and reproductive competence across multiple species, including the mare. By contrast, although prostaglandin F2 α (PGF2 α) also increases around ovulation, its functional significance remains less clearly defined, and it may represent a downstream metabolic product of enhanced PGE2 synthesis rather than a primary mediator of ovulatory events (Dozier et al., 2008).

Medical treatment aims to suppress ovarian activity and oestrogen production by the ovarian theca and granulosa cells. It is effective for acute or moderate mittelschmerz and for unruptured follicles. In women, mittelschmerz may improve with oral contraceptive use (Jensen & Speroff, 2000). In clinical practice, several protocols are available to suppress oestrus and associated behavioural signs in mares, although their efficacy may vary between individuals. Oral administration of altrenogest (0.044 mg/kg bwt once daily) is the most used approach, providing reliable suppression of oestrus behaviour within 2–3 days of initiation. Treatment is typically continued for the desired period of suppression, particularly in performance mares, but requires strict daily compliance (Lofstedt, 1988; Lofstedt & Patel, 1989; Perkins, 1999).

Longer-term suppression strategies include the induction of a prolonged luteal phase through the administration of long-acting progesterone formulations or the use of intrauterine devices, such as glass marbles, to mimic pregnancy and inhibit cyclicity (Nie et al., 2001). However, the efficacy of intrauterine devices is variable and may be associated with complications, including uterine irritation or expulsion.

Immunisation against gonadotropin-releasing hormone (GnRH) represents an alternative approach, inducing suppression of ovarian activity by reducing gonadotropin secretion (Garza et al., 1986; Safir et al., 1987; Schanbacher & Pratt, 1985; Tshewang et al., 1997). Although effective in decreasing ovarian function, treated mares may still exhibit oestrus-like behaviour, limiting its usefulness in cases where behavioural control is the primary objective (Dalin et al., 2002). Before embarking upon suppression of oestrus as a treatment for behavioural or performance issues in mares, veterinarians should verify the correlation between the mare being in oestrus and the occurrence of episodes of pain, behaviour abnormalities or poor performance (Hornberger et al., 2017). Suspending cyclic activity may benefit the rare mare in which discomfort is irregularly associated with multiple oestrous periods each season (Hornberger et al., 2017).

From a clinical perspective, the management of ovarian pain in mares is primarily based on the use of analgesic and anti-inflammatory drugs, although evidence-based protocols remain limited. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most employed agents, aiming to reduce prostaglandin synthesis and alleviate peri-ovulatory discomfort. Flunixin meglumine (1.1 mg/kg bwt, intravenously or orally, once to twice daily) and phenylbutazone (2.2–4.4 mg/kg bwt, orally, once to twice daily) are widely used in equine practice for the management of visceral pain and may provide short-term relief in cases of suspected ovarian discomfort (Mercer et al., 2023). However, the use of NSAIDs during the peri-ovulatory period must be approached with caution. Inhibition of prostaglandin synthesis can interfere with ovulation. Treatment with PG synthase inhibitors, NSAIDs or PG receptor antagonists, as well as genetic deletion of PG synthases, has been associated with anovulation and infertility in women and animal models (Bata et al., 2006; Duffy, 2015; Duffy et al., 2019; Duffy & Stouffer, 2002; Hester et al., 2010; Killick & Elstein, 1987; Lim et al., 1997; McCann et al., 2013; Pall et al., 2001). In mares, the administration of flunixin meglumine in the peri-ovulatory period also blocks ovulation and induces the development of luteinised unruptured follicles (Bashir et al., 2016; Cuervo-Arango, 2012; Cuervo-Arango & Domingo-Ortiz, 2011). For this reason, analgesic treatment is best reserved for mares not intended for immediate breeding or should be carefully timed in relation to the ovulatory cycle.

Adjunctive analgesic strategies may include the use of alpha-2 adrenergic agonists (e.g. xylazine, detomidine or romifidine) for short-term control of acute discomfort, particularly in cases presenting with colic-like signs, although their use is limited to supervised clinical settings (Gitari et al., 2017). Spasmolytic agents and mild sedatives may also be considered in selected cases to reduce visceral discomfort.

Importantly, analgesic therapy should be regarded as a symptomatic approach and does not address underlying causes of ovarian pain. Persistent or recurrent signs warrant further diagnostic investigation to exclude pathological conditions such as ovarian neoplasia or inflammatory processes. In clinical practice, a combined approach integrating pain management with hormonal suppression may be required in selected cases, depending on the severity and recurrence of clinical signs.

Although medical treatment may provide temporary suppression of hormone secretion and alleviate abdominal discomfort, bilateral ovariectomy may be considered in selected cases requiring definitive management. The procedure is generally performed either by standing laparoscopy or by laparotomy with the patient in dorsal recumbency and has been applied in mares and mules, to suppress unwanted oestrus behaviour and to decrease visceral pain occurring during oestrus (Giambrone et al., 2024; Hendrickson, 2012; Petrizzi et al., 2020; Röcken et al., 2011; Vullo et al., 2021). The technique is considered definitive in resolving mittelschmerz and different analgesic protocols are highly effective to reduce intra and postoperative pain at the ovarian site.

Adequate pain management is a critical component of ovariectomy in mares, both to ensure animal welfare and to optimise surgical

outcomes. Intraoperative analgesia is typically achieved through a multimodal approach combining sedation, local or regional anaesthesia and systemic analgesics. Standing laparoscopic ovariectomy commonly involves the use of alpha-2 adrenergic agonists (e.g. detomidine, xylazine or romifidine) in combination with opioids such as butorphanol or morphine, providing both sedation and visceral analgesia. In addition, local infiltration of lidocaine at the portal sites and mesovarian structures, as well as epidural administration of lidocaine with or without xylazine, may be employed to enhance intraoperative analgesia and reduce nociceptive responses (Giambrone et al., 2024).

Postoperative pain management generally relies on nonsteroidal anti-inflammatory drugs (NSAIDs), with flunixin meglumine (1.1 mg/kg bwt once or twice daily) or phenylbutazone (2.2–4.4 mg/kg bwt once or twice daily) administered for several days following surgery (Johnson et al., 1993), depending on the invasiveness of the procedure and the individual response of the mare. Multimodal analgesia may be continued in the immediate postoperative period, particularly in cases involving laparotomy or complications (Mama & Hector, 2019). Opioids are less commonly used postoperatively in horses but may be considered in selected cases under close supervision.

Minimally invasive approaches, such as standing laparoscopy, are associated with reduced postoperative pain, faster recovery and fewer complications compared to open techniques, further emphasising the importance of surgical technique in pain management (Hendrickson, 2012). Nevertheless, individual variation in pain perception and response to treatment should be considered, and analgesic protocols should be tailored accordingly.

Unilateral ovariectomy may be effective in cases of pathological conditions (neoplasm, haematomas, abscesses) (Carluccio et al., 2020). Drainage (transvaginal, transcutaneous, laparoscopic) can be attempted for conditions such as ovarian haematomas, which, although rare, can reach significant sizes and typically resolve spontaneously but may require surgical management in complicated cases (Carluccio et al., 2020). Ovarian abscesses can be aspirated but need antibiotic therapy following antibiogram from the aspirated material (Fernández-Hernández et al., 2024).

Regarding the oestrus-related behavioural abnormalities, more specifically, the actual benefit of ovariectomy is quite controversial. Mares are unique among domestic animals because in addition to the ovarian-derived oestrogen-induced signs of oestrous behaviour described above, many seasonally anovulatory (and ovariectomised) mares exhibit paradoxical oestrous behaviour associated with hormone secretion from the adrenal cortex (Hornberger et al., 2017). In a retrospective study of 35 cases, including 12 unilateral ovariectomies for pathology and 23 bilateral ovariectomies, ovariectomy resulted in continued displays of sexual receptiveness in all mares with a loss of normal cyclic activity. Ovariectomised mares showed more days of oestrus compared with when they were intact; 44 days of oestrus for all intact mares compared with 152 days for all ovariectomised mares during the study period. One ovariectomised mare showed 78 consecutive days of oestrus (Hedberg et al., 2007). This finding is supported by earlier observations that ovaries are not essential for oestrus

behaviour in the mare (Asa et al., 1980; Wesson & Ginther, 1981). Hooper et al. (1993) reported that 35% of mares demonstrated continued oestrus behaviour. In 9% of cases, this was judged to be 'objectionable' by the owners. Of 12 performance mares, 10 were judged to be competing at greater than preoperative levels. In another study (Kamm & Hendrickson, 2007), 22% of owners reported that they were either impartial or dissatisfied, mainly due to a failure of behavioural change following surgery. More generalised behavioural problems were more likely to be corrected with an ovariectomy than more specific behavioural issues. Aggressive behaviour and a generalised disagreeable demeanour were most corrected (86% and 81%, respectively), followed by excitability (75%), kicking and biting (73%) and problems during training that related to oestrus-like behaviour (72%). Problems with other horses and frequent urination were less likely to be improved after surgery (64%). None of the studies addressed the concept of ovarian pain as a cause of subtle behavioural issues encountered in ridden competition horses.

The current data would suggest that if the undesirable behaviour, which prompts presentation is normal sexual (oestrus) behaviour, then the likelihood is that ovariectomy will not correct the problem. In fact, ovariectomy may make the situation worse as oestrus behaviour may become irregular and/or persistent post-surgery. If the behaviour is aggressive in character, then ovariectomy is more likely to be a successful therapy, but the evidence for this is weak. It is advisable to evaluate the mare's response to nonsurgical methods of inducing ovarian quiescence (such as GnRH vaccination) before proceeding to surgery – if oestrous behaviour is not significantly reduced by medical treatment, it is unlikely to improve following surgery (Hornberger et al., 2017).

CONCLUSION

Ovarian pain associated with the peri-ovulatory period in the mare is a clinically relevant but likely underrecognised condition. Drawing from the well-established concept of mittelschmerz in women, a comparable physiological mechanism may contribute to transient discomfort, colic-like signs and behavioural changes observed in mares around ovulation. However, current evidence remains limited, and the distinction between physiological ovarian pain and pathological conditions continues to represent a major diagnostic challenge in equine practice.

A key clinical implication is the need for a thorough and multimodal diagnostic approach. Ovarian sensitivity detected during palpation or behavioural alterations during oestrus should not be automatically attributed to normal reproductive activity. Instead, clinicians should systematically exclude nonreproductive causes of pain and consider both non-neoplastic and neoplastic ovarian disorders. The overlap in clinical presentation and ultrasonographic findings highlights the importance of integrating clinical examination, imaging and, when appropriate, hormonal evaluation.

From a therapeutic perspective, treatment strategies must be carefully tailored to the individual mare. Medical suppression of

ovarian activity may provide temporary relief of discomfort and behavioural signs, but its effects are often inconsistent. While ovariectomy represents a definitive solution for ovarian pain, its impact on behaviour is variable and should not be considered a guaranteed outcome, particularly in cases where behavioural issues are not clearly linked to ovarian pathology.

Overall, greater awareness of ovarian pain as a potential contributor to clinical and behavioural signs in mares is essential. Future research is needed to better define its prevalence, pathophysiology and clinical significance, as well as to establish evidence-based guidelines for diagnosis and management. Improved understanding of this condition will support more accurate clinical decision-making and help avoid both underdiagnosis and overtreatment in equine patients.

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G. Marino: Conceptualization; writing – original draft. **V. Biondi:** Writing – review and editing. **A. Sfacteria:** Writing – review and editing. **G. Catone:** Writing – review and editing. **C. Vullo:** Conceptualization; writing – original draft.

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