

Face2Vet

A Clinical Update

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Smooth Calving – A pre-requisite for Healthy Dam and Foetus

Birth Without Barriers Facilitating Smooth Calving

Dear Vets,

Smooth calving is fundamental to reproductive efficiency, animal welfare and farm profitability. Successful parturition depends on coordinated interplay of endocrine events, effective uterine contractions, cervical ripening and dilatation, relaxation of soft birth canal, and proper foetal disposition. When this intricate process is disrupted, labour may become prolonged or difficult, leading to dystocia, compromised calf viability, maternal trauma and reduced subsequent reproductive performance.

Among various factors influencing calving success, adequate cervical ripening and birth canal compliance play a critical role in facilitating normal foetal delivery. Incomplete cervical dilatation, increased birth canal resistance and poor coordination between uterine contractions and cervical relaxation are important causes of functional dystocia that delay labour progression and increase the risk of obstetrical complications.

Effective management of dystocia requires timely diagnosis, careful obstetrical evaluation and appropriate intervention. A systematic approach involving correction of underlying metabolic disturbances, supportive therapeutic measures and proper case selection can significantly improve calving outcomes. As part of such an approach, Denaverine hydrochloride, through its cervical relaxant and birth canal compliance enhancing effects, can serve as a valuable supportive aid in facilitating labour progression and easing foetal delivery.

This issue of Face2Vet covers the physiology of parturition, mechanisms of cervical ripening and birth canal preparation, causes of dystocia and role of cervico-dilator as a supportive aid for facilitating smoother calving.

We invite you to read this issue and share your valuable feedback and thoughts by scanning the QR code below or by writing to us at face2vet@intaspharma.com.

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Introduction

Efficient reproductive management depends not only on successful conception and pregnancy maintenance but also on safe completion of parturition. A normal smooth and timely calving is essential for maintaining reproductive efficiency, animal welfare and farm profitability. Successful parturition results in delivery of viable calf, minimises trauma to dam, promotes rapid postpartum recovery and uterine involution and supports subsequent fertility.

Parturition is a complex physiological process involving coordinated endocrine activation, myometrial contractions, cervical ripening and dilatation, relaxation of vagina and vulva and correct foetal orientation. Successful delivery depends on the synchronization of these events. Disruption of any component may lead to difficult calving (dystocia), increasing the risk of maternal trauma, retained foetal membranes, metritis, reduced fertility and compromised calf viability.

Dystocia may arise from mechanical causes, such as foetal oversize or malpresentation, or functional causes, where labour fails to progress despite normal foetal positioning. Among functional causes, incomplete cervical dilatation and increased resistance of birth canal are important contributors to prolonged labour. Effective calving management therefore requires timely diagnosis and appropriate intervention. In cases of functional dystocia, reducing soft birth canal resistance and improving cervical compliance can facilitate smooth labour progression.

Physiology of Parturition

Endocrine Regulation of Parturition

Parturition is initiated and regulated by a coordinated endocrine cascade involving the foetus, placenta and dam. Hormonal changes not only trigger uterine contractions but also promote cervical ripening, pelvic relaxation and increased compliance of birth canal, all of which are essential for successful delivery.

Foetal Initiation of Parturition

Onset of labour is triggered by activation of foetal hypothalamic-pituitary-adrenal (HPA) axis. Rising foetal cortisol concentrations stimulate placental and maternal endocrine changes that shift reproductive tract from of pregnancy state to a state of

labour readiness. This shift includes reduced progesterone influence, increased estrogen activity, prostaglandin release, cervical ripening and increased myometrial responsiveness.

Progesterone Withdrawal and Estrogen Dominance

During pregnancy, progesterone maintains uterine quiescence by suppressing myometrial activity, inhibiting prostaglandin release and maintaining cervical closure. As parturition approaches, luteolysis and functional progesterone withdrawal occur, reducing its influence on target tissues.

Simultaneously, rising estrogen levels:

- Increase uterine excitability and contractility
- Enhance oxytocin receptor expression
- Promote coordinated uterine contractions through gap junction formation
- Stimulate cervical ripening and increase vascularity of reproductive tract

Insufficient estrogenic preparation may contribute to delayed or incomplete cervical dilatation.

Role of Prostaglandins

Prostaglandins are key mediators of labour progression:

- PGF₂α promotes luteolysis and uterine contractions
- PGE₂ facilitates cervical softening and ripening

Their actions include collagen remodelling, increased tissue hydration, vascular permeability and controlled inflammatory changes that transform the cervix into a soft and distensible structure.

Relaxin and Pelvic Preparation

Relaxin contributes to birth canal preparation by:

- Relaxing pelvic ligaments
- Increasing connective tissue elasticity
- Facilitating vulvar and perineal relaxation

Although these external changes indicate approaching parturition, they do not always reflect complete cervical dilatation.

Oxytocin and Ferguson Reflex

Oxytocin is the primary hormone responsible for strengthening and coordinating uterine contractions. As foetus enters the birth canal, cervical stretching activates the Ferguson reflex, stimulating oxytocin release from posterior pituitary. This positive feedback mechanism intensifies uterine contractions and promotes foetal expulsion.

Integrated Endocrine Control

Successful parturition depends on synchronized:

- Uterine contractions
- Cervical ripening and dilatation
- Relaxation of soft birth canal

Disruption of this coordination may result in delayed cervical dilatation, increased birth canal resistance and ineffective labour, leading to functional dystocia.

Mechanism of Parturition

Once the endocrine mechanism initiating parturition are activated, progressive uterine contractions, cervical dilatation and foetal descent lead to delivery of calf (Fig. 1). The process occurs in distinct stages, each characterised by specific clinical signs that aid assessment of labour progression and timely intervention when abnormalities arise.

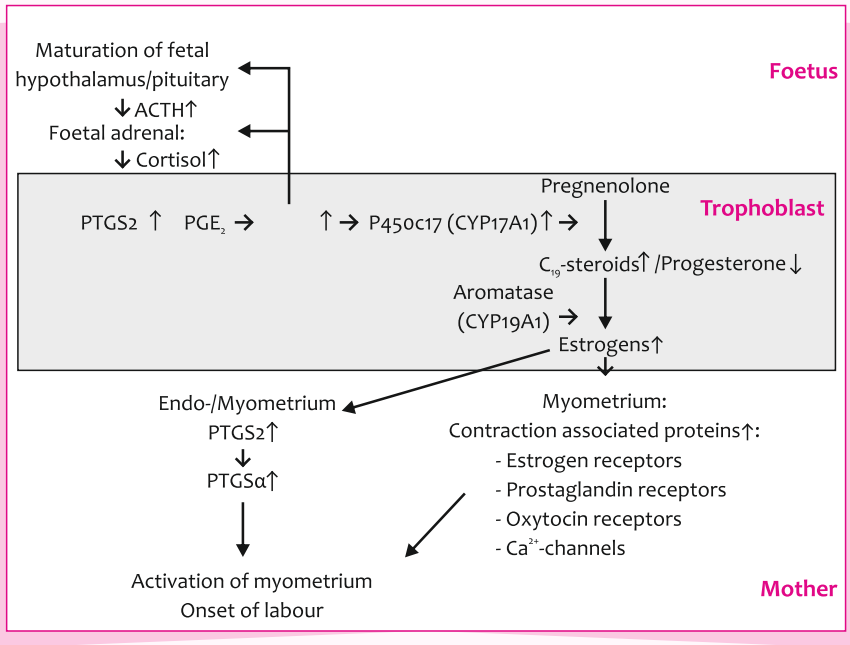


Fig. 1: Endocrine Events for Initiating Parturition
(Source: Whittle et al., 2001)

Stages of Parturition

Stage I: Cervical Dilatation

Stage I begins with the onset of uterine contractions and ends with complete cervical dilatation. It typically lasts 6–12 hours in cows and longer in heifers (Fig. 2).

Common signs include:

- Restlessness
- Frequent lying down and standing up
- Tail elevation
- Mucus discharge

During this stage, uterine contractions gradually soften and dilate the cervix in preparation for delivery.

Stage II: Expulsion of Foetus

Stage II begins once the cervix is fully dilated and ends with delivery of calf (Fig. 3). Strong uterine contractions and abdominal straining propel the foetus through birth canal. This stage usually lasts 1–2 hours in cows and up to 4 hours in heifers. Premature traction before adequate cervical dilatation increases the risk of cervical and vaginal trauma.

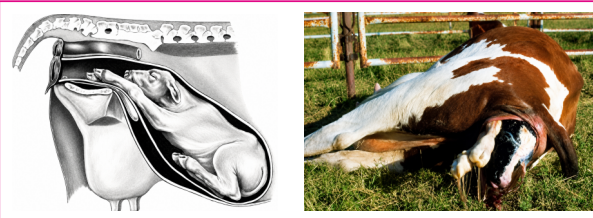


Fig. 3: Stage II of Parturition (Source: The Visual Guide to Bovine Reproduction Drost M. 1974)

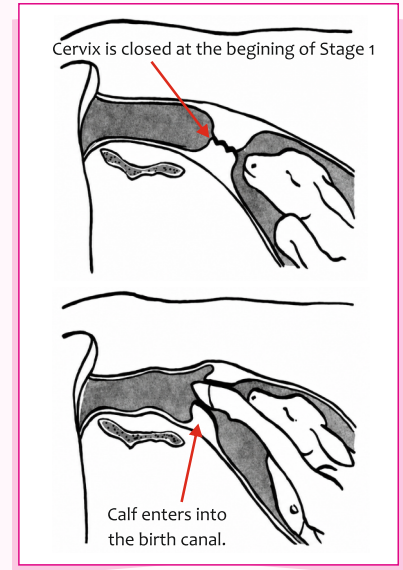


Fig. 2: Stage I of Parturition
(Source: Calving School Handbook - Beef Cattle Sciences, Oregon State University)

Stage III: Expulsion of Foetal Membranes

Stage III involves expulsion of placenta, which normally occurs within 4–8 hours after calving. Retention beyond 24 hours is considered abnormal and may impair further fertility.

Prolonged Stage I or Stage II labour is classified as dystocia. Difficult calving compromises calf viability through hypoxia and increases the risk of maternal trauma, exhaustion, postpartum disorders and reduced reproductive performance.

Cervical Ripening and Birth Canal Preparation

Structure and Function of Cervix

Cervix is the caudal portion of uterus and is composed primarily of dense connective tissue rich in collagen, proteoglycans and small amounts of smooth muscle. It performs multiple functions, including maintaining uterine sterility during pregnancy through formation of cervical plug and providing a passage for foetal delivery at parturition.

Cervical wall consists of:

- Outer layer: Tunica serosa
- Middle layer: Connective tissue interspersed with smooth muscle fibres
- Inner layer: Mucosal layer lined by secretory epithelial cells

During pregnancy, cervix remains firm and closed, but at calving it must dilate sufficiently to allow passage of foetus. Foetal pressure on cervix stimulates the Ferguson reflex, resulting in oxytocin release and stronger uterine contractions.

Cervical Ripening

Cervical ripening is not simply passive stretching. It is an active remodelling process. Prior to parturition, cervix undergoes a process known as cervical ripening, transforming it from a rigid structure into a soft, elastic and distensible birth canal.

This process involves:

- **Collagen Remodelling:** Reduction in collagen cross-linking and structural reorganization decreases tissue rigidity and improves extensibility.
- **Increased Tissue Hydration:** Accumulation of glycosaminoglycans, particularly hyaluronic acid, increases water content, softening the cervical tissue and reducing resistance.
- **Enzymatic and Cellular Changes:** Matrix metalloproteinases and inflammatory mediators promote breakdown and remodelling of extracellular matrix, facilitating cervical softening.

- **Smooth Muscle Relaxation:** Prostaglandins and nitric oxide reduce cervical smooth muscle tone, improving tissue compliance.

These changes are regulated by endocrine signals, particularly estrogen, prostaglandins, relaxin and oxytocin, which collectively prepare the birth canal for delivery.

Cervical Dilatation and Birth Canal Compliance

Following cervical ripening, coordinated uterine contractions and foetal pressure promote progressive cervical dilatation. Myometrial contractions generate the expulsive force required to open the cervix, while foetal descent into birth canal stimulates the Ferguson reflex, leading to increased oxytocin release and further strengthening of uterine activity.

Successful labour depends on a balance between:

- Adequate uterine force
- Minimal cervical and birth canal resistance

Weak uterine contractions may delay dilatation despite adequate ripening, whereas strong contractions acting against a poorly ripened cervix can prolong labour and increase the risk of tissue injury.

Causes of Incomplete Cervical Dilatation (ICD)

Hormonal Factors	Mechanical Factors	Soft Tissue Abnormalities	Uterine Factors
• Inadequate estrogen activity • Reduced prostaglandin response • Sustained progesterone signaling	• Pelvic abnormalities • Uterine torsion • Cervical fibrosis/ Cervical scarring	• Vaginal stenosis • Space occupying lesions	• Uterine inertia • Weak or uncoordinated contractions

Pathophysiology of Incomplete Cervical Dilatation (ICD)

Incomplete cervical dilatation is an important cause of functional dystocia in dairy animals, where labour fails to progress despite normal foetal disposition. It results from impaired cervical ripening, excessive cervical tone or poor coordination between uterine contractions and cervical relaxation, leading to increased resistance within the soft birth canal.

Major contributing factors include:

Failure of Cervical Ripening

Normal cervical dilatation depends on progressive softening and remodelling of cervical tissue. When this process is incomplete, the cervix remains firm, rigid and poorly distensible, creating resistance to foetal passage despite active uterine contractions.

Reduced Hydration and Elasticity

Adequate tissue hydration is essential for cervical compliance. Insufficient hydration results in a tight and inelastic cervical ring that delays or prevents complete dilatation.

Uterine Cervical Discoordination

Successful parturition requires synchronized uterine contractions and cervical relaxation. When strong uterine contractions occur before adequate cervical compliance is achieved, foetus is forced against a resistant cervix, prolonging labour and increasing maternal exhaustion.

Hypocalcaemia and Weak Uterine Activity

Calcium is essential for effective myometrial contractions. In animals with subclinical or clinical hypocalcaemia, weak uterine contractions reduce foetal pressure on cervix, slowing cervical dilatation and labour progression. While calcium therapy may restore uterine activity, it cannot correct intrinsic cervical rigidity or mechanical obstruction.

Premature or Forceful Traction

Premature traction can worsen incomplete cervical dilatation. When traction is applied before the cervix is fully dilated, foetus is forced against a resistant cervical ring, causing tissue trauma, inflammation and edema. Swelling reduces cervical elasticity and further impedes dilatation.

Excessive traction may lead to:

- | | | |
|--------------------------------|-----------------------|------------------------------|
| • Cervical and vaginal tears | • Uterine injury | • Foetal hypoxia |
| • Retained foetal membranes | • Postpartum metritis | • Delayed uterine involution |
| • Reduced subsequent fertility | | |

Hypertonicity of Birth Canal

Hypertonicity refers to excessive tone or spasm of cervix, vagina or other soft tissues of birth canal. Although foetus may be correctly positioned and uterine contractions may be adequate, delivery remains difficult due to increased soft tissue resistance.

Predisposing Factors of Dystocia

Dystocia is difficult or abnormal parturition requiring assistance and remains an important cause of calf loss, maternal injury and reduced reproductive performance. It results from abnormalities in dam, foetus or interaction between uterine forces and birth canal resistance. Maternal factors such as incomplete cervical dilatation and uterine dysfunction, along with foetal factors including oversize and malpresentation, are major contributors to dystocia. Nutritional deficiencies, metabolic disorders and environmental stress may further increase the risk.

Maternal Causes of Dystocia

- **Parity of dam:** Dystocia occurs more frequently in heifers than in mature cows due to smaller pelvic dimensions.
- **Incomplete cervical dilatation:** Failure of cervix to dilate adequately increases resistance to foetal passage and is a common cause of functional dystocia.
- **Narrow pelvis:** Limited pelvic space may result in foetopelvic disproportion and difficult parturition.
- **Uterine torsion:** Twisting of gravid uterus creates mechanical obstruction to foetal expulsion.
- **Uterine inertia:** Weak or ineffective uterine contractions prevent normal delivery despite cervical dilatation.

Foetal Causes of Dystocia

- **Foetal sex:** Male calves are generally larger and associated with a higher incidence of dystocia.
- **Foetal oversize:** A calf that is too large relative to the maternal pelvis is a major cause of difficult calving, particularly in heifers.
- **Abnormal foetal disposition:** Malpresentation, malposition and malposture interfere with normal passage through the birth canal and frequently necessitate obstetrical intervention.

Functional vs. Mechanical Dystocia

Traditionally, dystocia is classified as maternal or foetal in origin. However, from a practical obstetrical perspective, dystocia can also be categorized as functional or mechanical depending on whether labour is impaired by abnormal reproductive tract function or by a physical obstruction to foetal delivery. Differentiating between these forms is important because functional dystocia may respond to medical support, whereas mechanical dystocia requires obstetrical or surgical correction.

Table 1: Clinical Features of Functional and Mechanical Dystocia

Clinical feature	Functional dystocia	Mechanical dystocia
Primary cause	Inadequate cervical relaxation or ineffective uterine activity	Physical obstruction to foetal passage
Foetal size and posture	Usually, normal	Often abnormal, oversized or malpositioned
Cervix and birth canal	Tight, partially dilated or hypertonic	May be adequately dilated but obstructed
Uterine contractions	Weak, exhausted, excessive or poorly coordinated	Often strong but ineffective
Response to pharmacological support	May improve after appropriate examination and case selection	Limited benefit until obstruction is corrected
Main therapeutic approach	Supportive medical management with careful obstetrical monitoring	Obstetrical correction, controlled traction, fetotomy or caesarean section

General Therapeutic Approaches to Dystocia

Effective management of dystocia depends on accurate diagnosis and timely intervention. The choice of treatment is determined by whether the condition is functional or mechanical in origin.

Management of Mechanical Dystocia

Mechanical dystocia results from physical obstruction to foetal delivery and requires correction of underlying cause. Pharmacological therapy alone is ineffective and should not delay appropriate obstetrical intervention.

Management may include:

- Correction of foetal malpresentation or malposture.
- Controlled traction following confirmation of adequate cervical dilatation and correct foetal alignment.
- Foetotomy when vaginal delivery of a non-viable foetus is not possible.
- Caesarean section in cases of foetopelvic disproportion, uterine torsion or failed vaginal delivery.

Management of Functional Dystocia

Management of functional dystocia focuses on facilitating normal labour progression rather than applying forceful extraction. Initial measures include careful monitoring, adequate lubrication and correction of metabolic disturbances, particularly hypocalcaemia, which can impair uterine contractility. Calcium supplementation may improve uterine contractions but does not correct cervical rigidity or mechanical obstruction.

Pharmacological interventions may also be used:

- **Prostaglandins and corticosteroids** can aid cervical preparation and induction of parturition, although their usefulness is limited once active labour has begun.
- **Calcium supplementation** may improve cervical dilatation in animals with hypocalcaemia by enhancing myometrial contractions and increasing foetal pressure on the cervix.
- **Oxytocin** may be beneficial in uterine inertia but should only be used when adequate cervical dilatation is present.
- **Valethamate bromide (Epidosin):** Valethamate bromide is a spasmolytic quaternary ammonium compound with anticholinergic activity. Its mode of action is similar to atropine, producing peripheral smooth muscle relaxation. However, clinical responses may be variable, cervical relaxation may be incomplete and occasional anticholinergic adverse effects can occur.
- **Hyaluronan:** Hyaluronan acts by influencing tissue hydration and extracellular matrix changes. However, it has limited direct smooth muscle relaxant activity and may not provide rapid cervical relaxation during active labour.
- **Phosphodiesterase (PDE) inhibitors** such as Papaverine, Drotaverine and **Denaverine** promote relaxation of cervical and birth canal smooth muscles by increasing intracellular cAMP and cGMP concentrations, thereby reducing soft tissue resistance during labour.

Role of Denaverine Hydrochloride in Smooth Calving

Denaverine hydrochloride (DH) is a synthetic spasmolytic agent belonging to the Benzoic acid derivative group. Chemically, Denaverine hydrochloride has the molecular formula $C_{24}H_{34}ClNO_3$ and a molecular weight of 420.0 g/mol.

Mode of Action

- Denaverine hydrochloride is a phosphodiesterase (PDE) inhibitor with neurotropic and muscolotropic spasmolytic activity.
- By inhibiting phosphodiesterase, it prevents the breakdown of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), resulting in increased intracellular levels of these second messengers.
- Elevated cAMP and cGMP concentrations reduce intracellular calcium availability, leading to relaxation of smooth muscles in cervix, vagina and soft birth canal.
- Denaverine also relaxes smooth muscles within blood vessel walls, causing vasodilation and improved blood flow to reproductive tissues, which may further support cervical relaxation and labour progression.
- Overall effect is reduced soft tissue resistance, improved cervical compliance and enhanced distensibility of birth canal, facilitating foetal passage during labour.

Pharmacokinetics

- Rapid onset of action, generally within 15–30 minutes following intramuscular administration.
- Produces sustained relaxation of cervical and soft birth canal tissues for several hours, supporting labour progression.
- Extensively metabolized in the liver through ester cleavage, O-dealkylation and N-dealkylation pathways.
- Metabolites and unchanged drug are eliminated predominantly *via* urinary route.
- No evidence of clinically significant tissue accumulation following therapeutic administration.

Clinical Applications

- Denaverine hydrochloride is primarily indicated as a supportive aid during parturition and in animals experiencing functional dystocia associated with incomplete cervical dilatation, cervical spasm or increased resistance of soft birth canal.

- Following appropriate obstetrical evaluation and exclusion of mechanical causes of dystocia, administration of Denaverine hydrochloride, (**Denarin-Vet**) facilitates cervical relaxation, improve birth canal distensibility and support smoother foetal delivery.
- Following successful correction of uterine torsion, Denaverine hydrochloride (**Denarin-Vet**) may be administered when inadequate cervical dilatation persists, supporting cervical relaxation and improving readiness of the birth canal for vaginal delivery.
- In cases involving evacuation of retained, aborted, mummified or macerated fetuses, where insufficient cervical opening or excessive soft birth canal resistance hinders obstetrical procedures, Denaverine hydrochloride serve as a supportive aid by facilitating cervical relaxation and improving access to the reproductive tract.

The drug is administered by the intramuscular (IM) route. Commonly recommended doses include 400 mg in cattle and buffaloes, 80–120 mg in sheep and goats. In large animals, a repeat administration may be considered when adequate cervical dilatation has not been achieved following the initial treatment and clinical reassessment indicates continued need for cervical relaxation.

Clinical Evidences on Efficacy of Denaverine Hydrochloride

Study 1: Influence of Denaverine Hydrochloride on Calving Ease in Holstein Friesian Heifers (Lange *et al.*, 2019)

Objectives

To evaluate the effect of Denaverine hydrochloride on calving ease by assessing pulling force, duration of calving and stress response in Holstein Friesian heifers.

Materials and Methods

A randomized, placebo controlled, blinded trial was conducted on 83 Holstein Friesian heifers. Animals received either 400 mg Denaverine hydrochloride (n = 41) or placebo (n = 42), administered 30 minutes after the onset of active labour. Pulling force during assisted calving, duration of calving and serum cortisol concentrations were recorded.

Results and Discussion

Out of 83 heifers, 36 calved unassisted and 47 required assisted delivery. Denaverine hydrochloride significantly reduced the traction force × time (AUC) required during assisted calving ($64,373 \pm 50,514$ Ns vs. $91,553 \pm 61,886$ Ns in the placebo group; $P = 0.035$), indicating reduced birth canal resistance. The duration of calving assistance was numerically shorter in the Denaverine group (3.1 vs. 4.0 minutes). Denaverine hydrochloride improved calving ease by significantly reducing the force required for calf extraction during assisted delivery. The findings suggest improved cervical and birth canal compliance, supporting its use as a valuable obstetrical aid for ensuring smooth calving.

Study 2: Comparative Evaluation of Cervical Dilators for Management of Incomplete Cervical Dilatation (ICD) in Bovines (Sagar *et al.*, 2026)

Objectives

To compare the efficacy of Denaverine hydrochloride and Valethamate bromide in the management of incomplete cervical dilatation (ICD), a major cause of maternal dystocia in cattle and buffaloes.

Materials and Methods

A total of 30 bovines diagnosed with incomplete cervical dilatation (ICD) following full term gestation and failure of foetal delivery were included in the study. Animals were allocated to two treatment groups:

- Valethamate bromide (n = 10)
- Denaverine hydrochloride (n = 20)

Clinical examination and vaginal assessment of cervical dilatation were performed before treatment, followed by assisted delivery after administration of the cervical dilators.

Results and Discussion

Out of 30 bovines affected with incomplete cervical dilatation (ICD), 24 (80%) were buffaloes and 6 (20%) were cows. Compared with Valethamate bromide, Denaverine hydrochloride demonstrated superior efficacy in facilitating cervical dilatation and improving calving outcomes. Animals treated with Denaverine showed better cervical relaxation, enhanced birth canal compliance and a higher proportion of live calf deliveries. Overall, 15 of 24 buffaloes (62.5%) and 2 of 6 cows (33.3%) delivered live calves, with more favourable outcomes reported in the Denaverine treated group. Improved response was attributed to the potent spasmolytic action of Denaverine, which reduced cervical resistance and facilitated foetal passage. In addition, Denaverine was well tolerated and associated with minimal adverse effects. Denaverine hydrochloride was more effective than Valethamate bromide in managing incomplete cervical dilatation in cattle and buffaloes. Its superior cervical relaxant action facilitated easier calving and improved foetal survival, supporting its use in functional dystocia associated with ICD.

Conclusion

Successful calving depends on the precise coordination of hormonal events, effective uterine contractions, cervical ripening and adequate birth canal relaxation. When this coordination is disrupted, particularly due to incomplete cervical dilatation or increased soft birth canal resistance, functional dystocia may occur, adversely affecting calf viability, dam health and subsequent reproductive performance. Early diagnosis, correction of underlying metabolic disturbances and appropriate obstetrical management are essential for achieving favourable calving outcomes.

Denaverine Hydrochloride serves as a valuable supportive aid during parturition and in animals experiencing functional dystocia by promoting cervical relaxation and improving birth canal compliance without interfering with normal uterine contractions. When used following proper clinical evaluation and exclusion of mechanical causes of dystocia, it facilitates smoother labour progression, reduce delivery related trauma and contribute to improved maternal and neonatal outcomes.

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