Anaesthetic management of a bovine for ventral midline coeliotomy approach to hysterotomy

Abdur Rahmaan Kadwa*, Geoffrey James Brown and Roxanne Buck

Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria, South Africa

*Correspondence
Dr A.R. Kadwa, Private Bag x04, Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria, Onderstepoort, Gauteng, 0110, South Africa. Email: abdur.kadwa@up.ac.za

ABSTRACT

An eight-year-old, multiparous Chianina cow presented for the removal of a term, emphysematous calf following a dystocia. Delivery of the calf trans-vaginally intact or piecemeal by fetotomy was impossible due to the partially closed cervix. A midline coeliotomy approach to hysterotomy under general anaesthesia was elected in order to reduce peritoneal spillage of uterine content. This case report aims to discuss the peri-anaesthetic management of the cow, specifically the ventilation strategy, approach to premedication and analgesic protocol.

Keywords: α2 -adrenoceptor agonist, analgesia, cow, foetotomy, ketamine, oxygenation, uterus, ventilation

BACKGROUND

A full-term emphysematous fetus, retained in utero proximal to an insufficiently dilated cervix, is an occasional sequel to a neglected bovine dystocia. Since the dam may be medically compromised by septic uterine content, such cases are often best resolved pragmatically by euthanasia or emergency slaughter. However, in some instances, owners may wish to preserve the animal for future breeding. In such cases, the looming possibility of septicaemia imposes a dimension of urgency on case management. Hence, the surgical removal of uterine content may be considered.

Adult bovines are not ideal candidates for general anaesthesia due to their predisposition to cardiopulmonary complications.[1, 2] Thus, surgical interventions are often preferentially carried out under sedation and local anaesthesia.[3-5] However, general anaesthesia provides the advantage of reliable recumbency over longer periods of time and offers better control over the airway and cardiovascular status.[6, 7]

This case report will discuss important considerations in the anaesthetic management of a cow for undergoing hysterotomy via a ventral midline coeliotomy approach.

CASE PRESENTATION

An eight-year-old, 677 kg, multiparous Chianina cow was referred to the theriogenology service at the Onderstepoort Veterinary Academic Hospital, Pretoria, South Africa for the removal of a term, emphysematous foetus diagnosed by a referring veterinarian. Onset of labour was unobserved and occurred approximately a week prior to presentation.

On presentation, the cow was ambulatory, alert and responsive. Her clinical parameters were within normal limits and a copious, foetid vulvar discharge was noted. Manual examination of the reproductive tract revealed an obstructive dystocia due to faulty fetal disposition, resulting in a secondary inertia, oedema of the reproductive tract and constriction of the cervix. The tall stature and deep abdomen of the cow, together with a partially closed cervix, rendered fetotomy impossible. Thus, after discussion with the owner, a ventral midline coeliotomy under general anaesthesia was elected, to limit peritoneal contamination. Pre-operatively, a complete blood count (ADVIA 2120, Siemens Healthineers) and biochemistry panel (COBAS INTEGRA® 400 plus, Roche) were performed. Abnormal results included a mild normochromic, normocytic anaemia, haematocrit of 0.23 (0.24–0.40), a mild monocytosis 1.14×10^9/L (0.03–0.84), 2+ piroplasmosis (*Babesia* species) and a mild hypoalbuminaemia 25.1 g/L (31–43).

TREATMENT

Routine preoperative fasting was not instituted due to the urgent nature of the case. Delay in removing the uterine contents may have progressed to a septicaemia and potential decline in the cardiovascular status of the animal.

For induction, the cow was secured to a tilting table equipped with a neck clamp. A 20G, over-the-needle, intravenous catheter (Jelco, Smiths Medical) was placed into the right auricular vein. The induction sequence consisted of 0.1 mg/kg diazepam (Pax, Aspen Pharmacare) and 2 mg/kg ketamine (Ketamine-Fresenius, Fresenius-Kabi). A further 2 mg/kg ketamine (administered over three boluses) and 0.07 mg/kg diazepam was required to achieve adequate anaesthetic depth for endotracheal intubation. Once the cow had lost consciousness, the cow was strapped to the table and subsequently tilted. Intubation was achieved by placing a Drinkwater's mouth-gag into the right molar arcade and thereafter railroading a cuffed, 24-mm internal diameter, silicone, endotracheal tube (Jorvet, Jorgensen Laboratories) over a stomach tube previously placed into the trachea by trans-oral palpation of the larynx. Copious regurgitation (approximately 20 L of rumen content) occurred immediately after intubation and inflation of the cuff of the endotracheal tube with 50 mL of air. The animal was connected to an anaesthetic machine with incorporated time-cycled ventilator (Dräger Narkovet-E Electronic Large Animal Control Center, North American Dräger). Isoflurane (Isofor, Safeline) in oxygen was administered; the tidal volume was set at 7 L resulting in a peak inspiratory pressure of 25 cm H_2O, respiratory rate of 10 breaths per minute and an oxygen flowrate of 10 L/min.

The cow was positioned in dorsal recumbency with the hindquarters rotated 45° to the right to facilitate exteriorisation of the uterus. Sandbags were placed under the poll to facilitate drainage of saliva. An over the needle intravenous catheter (12G; Intraflon, Kruuse) was placed into the left external jugular vein to facilitate administration of 15 L of a balanced crystalloid solution (Lactated Ringers' Solution, Fresenius-Kabi) over the course of the anaesthetic period. A 20G over the needle intravenous catheter (Jelco, Smiths Medical) was placed into the right auricular artery, to facilitate direct arterial blood pressure measurement and sampling for blood gas analysis.

A multiparametric monitor (Cardiocap/5, Datex-Ohmeda) was used to obtain side-stream sampling of respiratory gasses to measure end-tidal carbon dioxide partial pressure (Pe'CO_2) and anaesthetic agent concentration, three-lead ECG in a base-apex configuration to detect cardiac electrical activity and invasive blood pressure via a strain-gauge transducer (BD TDX, Becton Dickinson, (Pty), Ltd) zeroed to atmospheric pressure at right atrial level. Physical monitoring included the reactivity of the palpebral reflexes, degree of eyeball rotation and presence of nystagmus. The oxygen flow rate was reduced to 7 L/min and vapouriser output adjusted between 2.5% and 3.5% (v/v) to maintain an end-tidal anaesthetic concentration of 1.6−1.9%. The respiratory rate was set at 6 breaths/min. A pipe connected to the expiratory valve of the ventilator was submerged in water to provide a positive end expiratory pressure (PEEP) of 8 cmH_2O.

A single dose of butorphanol (Dolorex, Merck Animal Health) was administered at 0.02 mg/kg intravenously to provide analgesia. An upward trend in the blood pressure (> 130 mmHg systolic blood pressure) was interpreted as a pain response, signifying insufficient analgesia. A ketamine constant rate infusion was initiated at 0.1 mg/kg/h and titrated to 0.15 mg/kg/h at which point it seemed to provide sufficient analgesia. Three boluses of lidocaine (Lidocaine 2%, Bayer) at 0.3 mg/kg were administered intravenously, 60 minutes apart to provide additional analgesia. Oxytocin, (2000 IU intravenously and 2000 IU intramuscularly, Fentocin, Virbac) was administered to facilitate uterine involution after closure of the uterus.

Arterial blood gas analysis was performed twice, 30 minutes after induction of anaesthesia and again 75 min later. The samples were drawn anaerobically into a heparinised syringe (BD A-Line, Becton Dickinson Ltd) and immediately analysed on a bench-top analyser (RAPIDPoint 500, Siemens Healthineers). The pH, PaO_2 and $PaCO_2$ remained within acceptable limits (Table 1). Twenty millilitres of calcium borogluconate 40% (Norcal 40 MP, Norbrook Laboratories) was infused over 20 minutes to treat the hypocalcaemia noted on the first blood gas analysis.

LEARNING POINTS/TAKE-HOME MESSAGES

- The anatomical and physiological characteristics of cattle specific to anaesthesia should be considered in context of the case presentation.
- Ventilation technique should be individualised depending on comorbidities, to maintain adequate oxygenation.
- Furthermore, the use and choice of specific α2-adrenoreceptor agonists should be weighed against the clinical scenario.
- Potential electrolyte imbalances should be investigated and treated accordingly, particularly when the risk of peritonitis and septicaemia is present.
- The provision of analgesia is extremely important in maintaining a high welfare standard as well as mitigating complications during the convalescence period.
- Local legislation with regard to use of drugs and withdrawal periods must be considered.

TABLE 1. Arterial blood gas parameters and ventilation calculations for a Chianina cow anaesthetised for midline coeliotomy approach to hysterotomy

Minutes after induction	30 min	105 min
Parameter	***Value***	***Value***
pH	7.382	7.301
$PaCO_2$	49 mmHg	56.9 mmHg
PaO_2	129.7 mmHg	147.5 mmHg
HCO_3^- (actual)	28.5 mmol/L	27.4 mmol/L
Base excess (ECF)	3.4 mmol/L	1.0 mmol/L
Oxygen saturation	98.5%	98.6%
PaO_2/ FiO_2	1.3 mmHg/%	1.55 mmHg/%
Na^+	137.1 mmol/L	136.8 mmol/L
K^+	4.29 mmol/L	4.58 mmol/L
Ca^{++}	1.07 mmol/L	1.12 mmol/L
Cl^-	104 mmol/L	104 mmol/L
Anion Gap	8.9 mmol/L	9.9 mmol/L
Lactate	1.96 mmol/L	0.9 mmol/L
$PE'CO_2$	49 mmHg	48 mmHg
$PaCO_2$-$PE'CO_2$ gradient	0 mmHg	8.9 mmHg
F-shunt	4.97%	4.85%

A 30 cm incision was made in the greater curvature of the pregnant uterine horn and the emphysematous fetus extracted. Limited spillage of uterine content occurred into the abdominal cavity. The uterus was closed with a single-layer inverting pattern. The abdominal cavity was copiously flushed with 30 litres of sterile, warm Lactated Ringers' Solution (Fresenius-Kabi South Africa) and suctioned to remove as much uterine spillage as possible. The midline abdominal incision was closed routinely.

During closure of the abdomen, the nasal and oral cavities were flushed with water and mopped out with abdominal swabs to remove as much regurgitated material as possible in order to limit the risk of an aspiration pneumonia.

Anaesthetic time was 210 minutes and surgery time was 137 minutes. Ten minutes after cessation of anaesthesia, the cow was positioned in sternal recumbency in a padded recovery stall. Mattresses were positioned on either side of it to prevent it rolling over. A smaller mattress was positioned underneath its mandible to support its head. The cow was extubated 16 minutes later, with the cuff partially inflated, when its swallowing reflex returned, and it was supporting its head. Forty-four minutes after extubation, the cow stood up and was guided to its stall in the large animal hospital.

Flunixin meglumine (2.2 mg/kg intramuscularly, Finadyne, MSD Animal Health Hub) was administered for post-operative analgesia, cloprostenol (500 µg/kg intramuscularly, Estrumate, Merck Animal Health) was administered to facilitate expulsion of remaining uterine contents and ceftiofur (2 mg/kg intramuscularly, Excenel RTU EZ, Zoetis) was administered to mitigate potential post-operative infection.

OUTCOME AND FOLLOW-UP

Two days post-operatively, a complete blood count was repeated. A mild inflammatory leukogram with moderately elevated band neutrophils 0.33×10^9/L (0–0.12) was noted.[8] The cow remained hospitalised for a further eight days to monitor for surgical site dehiscence and was subsequently uneventfully discharged.

The future profitability of this cow and return on investment (hospitalisation and surgical expenses) depends on its return to a normal oestrous cycle and rearing of a healthy calf.[9] It is unknown how the surgical intervention affected the future reproductive performance of the cow. Repeated attempts to contact the farmer in this regard were to no avail.

DISCUSSION

This case highlights three important learning points. Firstly, the effective ventilation strategy to maintain clinically acceptable arterial oxygenation in an unstarved cow carrying a term fetus, secondly the decision not to use α_2-adrenoreceptor agonists due to their effects on uterine tone and finally, the provision of analgesia by means of a ketamine constant rate infusion.

Adult cattle undergoing elective surgery are routinely starved prior to anaesthesia to minimise the risk of regurgitation and aspiration during the anaesthetic period.[10] Furthermore, starving prior to anaesthesia minimises the volume of ingesta within the gastrointestinal tract and diminishes the risk of bloat, thus limiting the impediment to diaphragmatic movement and venous return. Most resources recommend withholding food for 24−48 hours and water for a minimum of 12 hours.[1-5] In this case however, preoperative starvation was not instituted due to the urgent nature of the case. Delaying surgery placed the cow at increasing risk of uterine rupture and a resultant septic peritonitis and systemic inflammatory response syndrome. These factors outweighed the risks of not starving the cow, while giving it the best prognosis as a future breeding cow.

Cattle are at risk of regurgitation and aspiration of ruminal contents at light or deep planes of anaesthesia.[2, 10] Active regurgitation usually occurs due to pharyngeal stimulation during intubation in a lightly anaesthetised animal. As the anaesthetic period progresses and the plane of anaesthesia deepens, passive regurgitation occurs secondary to relaxation of the lower oesophageal sphincter.[2] Adequate preparation for intubation with a cuffed endotracheal tube, familiarity with the laryngeal anatomy and techniques of intubating adult cattle may mitigate the risk of aspiration.[2] Furthermore, the use of diazepam in the anaesthetic drug protocol may decrease the risk of regurgitation as it is purported to increase the tone of the lower oesophageal sphincter.[10]

Chianina are the largest cattle breed in the world,[11] thus a ventral midline celiotomy was considered a more viable option than a paralumbar fossa celiotomy for limiting peritoneal contamination[12], considering that the calf was severely autolysed and emphysematous at the time of presentation. Schultz and others[12] described the ventral midline approach to the abdomen of a cow under heavy sedation, however general anaesthesia was elected for to ensure to better control of the airway and thereby reduce the risk of aspiration.

The anatomy of the thoracic and abdominal compartments of cattle predispose them to cardiopulmonary compromise under general anaesthesia. The rumen, which accommodates up to 200 litres of fluid in the adult bovine, occupies approximately three-quarters of the abdomen.[2, 4] Abnormal positioning, especially in dorsal recumbency, impedes diaphragmatic movement and impairs venous return to the heart due to the weight of the abdominal contents placed on the large veins of within the abdomen.[1, 3, 4, 6] These factors, in combination with anaesthetic-mediated central depression of respiration predispose cattle to hypoxaemia and hypercapnoea under general anaesthesia.[1, 6, 10] Cardiopulmonary compromise can be further exacerbated in unstarved or heavily pregnant animals due to the increased size of the rumen or gravid uterus.[3, 6] In the present case, despite an unstarved cow carrying a term fetus, arterial oxygenation remained clinically acceptable.

Functional residual capacity (FRC) is the volume of gas remaining within the lungs after a normal tidal expiration.[13] Its purpose is to maintain the patency of the distal bronchioles and alveoli. Large animals, such as cattle and horses develop ventilation/perfusion (V/Q) mismatching within 20 min of induction of general anaesthesia,[14-16] represented by two extremes: ventilated but non-perfused alveoli ($V/Q = \infty$) and perfused but non-ventilated alveoli ($V/Q = 0$).[16] In horses, where ventilation under anaesthesia has been extensively investigated, the latter scenario usually occurs (a reduction in the V/Q ratio) due to the weight of the abdominal viscera overlying the diaphragm and reduction in the tone of the respiratory muscles.[15, 17] These factors result in the reduction of FRC such that alveolar closing volume exceeds FRC culminating in large areas of pulmonary atelectasis. Thus, the V/Q mismatching in horses under anaesthesia is due to the development of atelectasis when the animal is positioned in either lateral or dorsal recumbency. The mechanisms of atelectasis are threefold: compression atelectasis due to reduced transpulmonary pressure, absorption atelectasis as a result of greater uptake of gas into the blood compared to that entering the alveoli and decreased surfactant production due to the effect of inhalational agents on type II pneumocytes.[13, 15] Compression atelectasis however, is the major contributor.[15] Considering that the cow in question was unstarved and had a term fetus in its uterus, it is logical to assume that it likely developed large areas pulmonary atelectasis resulting in significant V/Q mismatching.

Collateral ventilation allows ventilation of alveoli via the pores of Kohn during instances of distal airway collapse. Cattle do not possess any of these channels within the anatomy of their respiratory tracts. Thus, the collapse of small airways in cattle results in the loss of the entire alveolar unit supplied by these airways thus resulting V/Q mismatching.[13]

Cattle, in comparison to other species, possess relatively muscular pulmonary arteries and arterioles.[18] Therefore, to compensate for a lack of collateral ventilation, cattle exhibit a potent hypoxic pulmonary vasoconstriction (HPV) reflex. This reflex is triggered in the face of a low alveolar partial pressure of oxygen in the alveoli and mixed venous blood directing blood away from alveolar units that are poorly ventilated.[13] Oxygen-sensitive, voltage-gated potassium channels in the walls of pulmonary vessels are inhibited, leading to an accumulation of potassium intracellularly, effecting a depolarisation of the cell. This depolarisation results in the opening of L-type calcium channels allowing a calcium influx causing vasoconstriction.[19] However, volatile anaesthetic agents inhibit this reflex in a dose dependant manner. As a result, in cattle and horses maintained under inhalational agents, some perfusion of poorly ventilated alveolar units occurs, thereby giving rise to a higher than physiological venous admixture.[13] The lack of collateral ventilation and depression of the

HPV reflex likely resulted in exacerbation of the V/Q mismatching already present in this case.

Further evidence for a reduced V/Q can be deduced from the $PaCO_2$ to $PE'CO_2$ gradient observed over time (Table 1). The gradient values were within limits of the minimum reported values for healthy and compromised horses under anaesthesia.[16, 20] In this case, the $PaCO_2$ increased in relation to the $PE'CO_2$ over time indicating reduced elimination of CO_2 into the alveoli, thus demonstrating a reduced V/Q ratio.[16] Evaluation of gaseous exchange is imperative to adequate management of ventilated patients, traditionally performed using oxygen tension-based indices.[21, 22] However, the F-shunt equation, a modification of the Berggren equation, an oxygen-content based index has been found to correlate better with venous admixture (Qs/Qt) in anesthetised horses and sheep.[21, 22] It assumes a fixed arteriovenous oxygen gradient of 3.5 mL/dL and is relatively easy to apply in clinical scenarios as follows:

$$\left[\left(Cc'O_2 - CaO_2\right)/\left(Cc'O_2 - CaO_2\right) + 3.5\right] \times 100$$

where CaO_2 is the arterial oxygen content and $Cc'O_2$ is the pulmonary capillary oxygen content (which is assumed to be 100% saturated with oxygen) and can be calculated as follows:[22]

$$(1.34 \times Hb \times 1.00) + (0.003 \times PaO_2)$$

where Hb is haemoglobin concentration and PaO_2 is partial pressure of arterial oxygen.

The F-shunt values calculated (Table 1) indicate a minimal degree of shunting when compared to an estimate of up to 33% pulmonary shunting in dorsally recumbent, anaesthetised horses[15] and 21.5% laterally recumbent sheep.[22] However, the calculated shunt F-shunt value should always be interpreted cautiously if there is reason to suspect a reduction in cardiac output.[21, 22] A marked reduction in Qs/Qt values in anaesthetised horses secondary to the application of PEEP has also been described.[23]

Although thoracopulmonary compliance was not measured in this case, it was assumed that the intra-abdominal pressure from the gravid uterus and full rumen decreased the FRC, resulting in some degree of atelectasis and thus decreased pulmonary compliance.[17] PEEP is a pre-set pressure during mechanical ventilation; it prevents the airway pressure from reaching atmospheric pressure at the end of a respiratory cycle.[13] PEEP stabilises alveolar units by increasing FRC above the closing volume, thus preventing closure of the small airways and subsequent alveolar collapse.[13] The application of PEEP thereby improves V/Q matching and thus oxygenation and also may effect an increase in pulmonary compliance.[13, 14, 17, 23]. Although the application of PEEP improves gaseous exchange, it may cause a reduction in cardiac output and mean arterial blood pressure (MAP), especially in hypovolaemic animals.[14, 23] Therefore, a conservative PEEP level of 8 cmH_2O was initially instituted and would have been titrated upward had the need arose. Although the minimum recommended PEEP level in horses is 10 cmH_2O,[17] the application of 8 cmH_2O PEEP in this case resulted in a clinically acceptable PaO_2 and the MAP remained within acceptable limits (70–90 mmHg) for the duration of anaesthesia.

A parallel can be drawn between the present case and a case described by Jurado and others,[24] where the anaesthetic management of a heavily pregnant cow presenting for surgical reduction of a metacarpal fracture was discussed. Contrary to the present case, positive pressure ventilation was not implemented due to a concern for hypotension occurring consequent to reduced venous return. Severe hypoxaemia ensued, ranging from a PaO_2 of 64 mmHg during the first hour of anaesthesia to 48 mmHg during the last hour of anaesthesia. In the present case, application of positive pressure ventilation with PEEP ensured adequate arterial oxygenation.

Cattle generally do not require sedation due to their docile nature, however α_2-adrenoreceptor agonists are used for their predictable sedative effects in fractious animals, dose-sparing effects on induction and maintenance agents, as well as providing analgesia.[2, 4, 10, 24] Generally, α_2-adrenoreceptor agonists are thought to increase myometrial contractility,[25] however, there may be different effects between drugs of this class. Xylazine is purported to increase uterine tone.[2, 3, 10, 25, 26] Conversely, detomidine has been reported to have either no effect on uterine tone or cause uterine relaxation in mares and cows,[2, 4, 10] although Gibbs and others[27] found it to increase uterine tone in non-pregnant mares. Schultz and others[12] recommend against the use of xylazine during caesarean sections due to its myotonic effects on the uterus. Increased uterine tone complicates exteriorisation of the uterus and increases friability of uterine tissue, escalating the likelihood of tears during closure.[12] Thus, α_2-adrenoreceptor agonists were not administered in this case, due to their variable effects on uterine tone; the induction and intubation sequence was completed with additional boluses of ketamine and diazepam. The effects of α_2-adrenoreceptor agonists on uterine tone are influenced by the concurrent hormonal milieu where a preponderance of oestrogen increases the sensitivity of uterine α_2-adrenoreceptors, increasing uterine contractility while a progesterone dominated environment sensitises uterine β-adrenoreceptors, promoting uterine relaxation.[25] In cattle, rising concentrations of oestrone sulphate from mid-pregnancy until the peri-parturient period[28] may promote increased uterine contractility when α_2-adrenoreceptor agonists are administered, and thus were avoided in this case. In cases where α_2-adrenoreceptor agonists are warranted, β-adrenoreceptor agonists may offset their myotonic effects. Jurado and others,[24] successfully employed isoxsuprine to offset the effects of xylazine on the uterus; a healthy calf was born at term. In addition to α_2-adrenoreceptor agonists, ketamine has also been reported to increase uterine tone in sheep[29, 30] therefore, the cow in this case may have benefited from the administration of a β-adrenoreceptor agonist. However, these drugs were not available on short notice at our institution.

The recognition and alleviation of pain in farm animals has received significant attention over recent years, in an effort to improve welfare in production animal systems.[31] Pain adversely affects an animal's quality-of-life[31] by inducing both emotional distress and pathophysiological states in multiple organ systems.[32] Visceral pain is considered to be the most painful clinical condition in cattle[32] and by extension, abdominal surgery is the most painful surgical procedure performed in cattle.[31] In this case, multimodal analgesia was provided by administering boluses of butorphanol and lidocaine and a constant rate infusion of ketamine intra-operatively, followed by flunixin meglumine post-operatively. Butorphanol was selected over morphine due to greater familiarity with its clinical effects and more widespread use in bovine medicine.[33, 34] Moreover, the side effect profile of butorphanol is more favourable than morphine: there is less risk of excitement and ileus during the post-operative period.[33, 34] From a pharmacological perspective, morphine, a μ-opioid receptor agonist is theoretically the most efficacious analgesic.[33, 34] However, Kalpravidh and others[35] found that butorphanol, a μ-opioid receptor antagonist and κ-opioid receptor agonist provided better visceral analgesia in horses as compared to morphine. Furthermore, Hartnak and others[31] found that a morphine, lidocaine and ketamine infusion compared to two doses of flunixin meglumine provided equivalent analgesia in calves undergoing umbilical herniorrhaphy. The analgesic protocol was likely sufficient, judging by the response of the blood pressure to the lidocaine boluses and titration of the ketamine infusion. Although an infusion of lidocaine may have provided more consistent analgesia, they are associated with increased ataxia and poor quality recoveries.[31] However, terminating the infusion prior to discontinuing the inhalational anaesthetic drug may mitigate the poor recovery quality.[31] Anderson and Muir[32] contend that NSAIDs form the cornerstone of multimodal analgesia in cattle. Administering flunixin meglumine pre-operatively in this case would have likely provided a better level of analgesia as NSAIDs reduce the development of central sensitisation in cattle,[36] however, this was neglected until recovery during the logistics of preparing for a bovine coeliotomy.

Hypocalcaemia is common in periparturient cows due to the sudden demand not being matched by homeostatic mechanisms.[37] Inhalational agents are non-specific calcium channel blockers and mediate their negative inotropic and vasodilatory effects by altering calcium ion flux. Therefore, the cardiovascular effects of inhalational agents are potentiated by hypocalcaemia[38] and thus careful monitoring and intervention is warranted in animals at risk for hypocalcaemia.

South African legislation (the Veterinary and Para-veterinary Professions Act, 19/1982) permits veterinarians the extra-label use of drugs if no alternate veterinary alternative is available. However, the Foodstuffs, Cosmetics and Disinfectants Act 54/1972 protects consumers from residues of veterinary drugs entering the human food chain by allowing the use of these drugs only if a withdrawal period has been set. In this light, Act 19/1982 dictates the withdrawal period for drugs used on an extra-label basis at 120 days. In this case, the extra-label administration of diazepam and ketamine limits the use of milk or meat from this animal until the specified withdrawal period has elapsed.

REFERENCES

1. Carrol GL, Hartsfield SM. General anesthetic techniques in ruminants. *Vet Clin North Am Equine Pract*. 1996; 12: 627- 61.
2. Greene SA. Protocols for anesthesia of cattle. *Vet Clin North Am Equine Pract*. 2003; 19: 679- 93.
3. Hubbel JAE, Hull BL, Muir WW III. Perianesthetic considerations in cattle. *Compend Contin Educ Vet*. 1986; 8: 92– 9.
4. McGregor RS, Jones RF. General anaesthesia of large animals. *Current Anaesthesia and Critical Care*. 1998; 9: 86– 91. https://doi.org/10.1016/S0953-7112(98)80034-3
5. Hallowell GD, White KL, Fishwick JC, *et al*. Clinical forum: General anaesthesia in cattle. *Livestock*. 2012; 17:30—-34. https://doi.org/10.1111/j.2044-3870.2012.00149.x
6. Tranquilli WJ. Techniques of inhalation anesthesia in ruminants and swine. *Vet Clin North Am Equine Pract*. 1986; 2: 593– 619. https://doi.org/10.1016/S0749-0720(15)31208-1
7. Arthurs OJ, Sury M. Anaesthesia or sedation for paediatric MRI: advantages and disadvantages. *Curr Opin Anesthesiol*. 2013; 26: 489- 94. https://scite.ai/reports/10.1097/aco.0b013e3283620121

8. Roland L, Drillich M, Iwerson M. Hematology as a diagnostic tool in bovine medicine. *J Vet Diagn Invest*. 2014; 26: 592- 8. https://doi.org/10.1177/1040638714546490
9. Goshu G. Breeding efficiency, lifetime lactation and calving performance of Friesian-Boran crossbred cows at Cheffa farm, Ethiopia. *Livestock Research for Rural Development*. 2005; 17: http://www.lrrd.org/lrrd17/7/gosh17073.htm
10. Dugdale A. Veterinary Anaesthesia Principles to Practice. 1st ed. Oxford: Wiley-Blackwell; 2010.
11. The Cattle Site. Cattle Breeds – Chianina. 2000. https://www.thecattlesite.com/breeds/beef/44/chianina/ (accessed 21 August 2020)
12. Schultz LG, Tyler JW, Moll D, *et al*. Surgical approaches for cesarean section in cattle. *Can Vet J*. 2008; 49: 565– 68.
13. Mosing M, Senior JM. Maintenance of equine anaesthesia over the last 50 years: Controlled inhalation of volatile anaesthetics and pulmonary ventilation. *Equine Vet J*. 2017; 50: 282- 91. https://doi.org/10.1111/evj.12793
14. Hopster K, Kästner SBR, Rohn K, *et al*. Intermittent positive pressure ventilation with constant positive end-expiratory pressure and alveolar recruitment manoeuvre during inhalation anaesthesia in horses undergoing surgery for colic, and its influence on the early recovery period. *Vet Anaesth Analg*. 2011; 38: 169- 77. https://doi.org/10.1111/j.1467-2995.2011.00606.x
15. Auckburally A, Nyman G. Review of hypoxaemia in anaesthetized horses: predisposing factors, consequences and management. *Vet Anaesth Analg*. 2017; 44: 397– 408. https://doi.org/10.1016/j.vaa.2016.06.001
16. Mosing M, Böhm SH, Rassis A, *et al*. Physiologic Factors influencing the arterial-to-end-tidal CO_2 difference and the alveolar dead space fraction in spontaneously breathing anesthetised horses. *Front Vet Sci*. 2018; 5: 1– 8. https://doi.org/10.3389/fvets.2018.00058
17. Andrade FSRM, Facó LL, Ida KK, *et al*. Effects of 12 and 17 cmH2O positive end expiratory pressure applied after alveolar recruitment maneuver on pulmonary gas exchange and compliance in isoflurane anesthetized horses. *Vet Anaesth Analg*. 2019; 46: 64– 73. https://doi.org/10.1016/j.vaa.2018.08.003
18. Heath D. Hypoxia and the pulmonary circulation. *J Clin Path*. 1977; 30: 21– 9. https://doi.org/10.1136/jcp.s3-11.1.21
19. Sarkar M, Niranjan N, Banyal PK. Mechanisms of hypoxemia. *Lung India*. 2017; 34: 47– 60. https://doi.org/10.4103/0970-2113.197116
20. Koenig J, McDonell W, Valverde A. Accuracy of pulse oximetry and capnography in healthy and compromised horses during spontaneous and controlled ventilation. *Can Vet J*. 2003; 67: 169– 74.
21. Briganti A, Portella DA, Grasso S, *et al*. Accuracy of different oxygenation indices in estimating intrapulmonary shunting at increasing infusion rates of dobutamine in horses under general anaesthesia. *Vet J*. 2015; 204: 351- 6. https://doi.org/10.1016/j.tvjl.2015.04.002
22. Araos JD, Larenza MP, Boston RC, *et al*. Use of the oxygen content–based index, Fshunt, as an indicator of pulmonary venous admixture at various inspired oxygen fractions in anesthetized sheep. *Am J Vet Res*. 2012; 73: 2013- 20. https://doi.org/10.2460/ajvr.73.12.2013
23. Ambrósio AM, Ida KK, Souto MTMR, *et al*. Effects of positive end-expiratory pressure titration on gas exchange, respiratory mechanics and hemodynamics in anesthetized horses. *Vet Anaesth Analg*. 2013; 40: 564- 72. https://doi.org/10.1111/vaa.12068

24. Jurado OM, Jud R, Muggli E, *et al*. Balanced anaesthetic approach in a late-term gravid cow undergoing metacarpal fracture repair. *Case Reports in Veterinary Medicine*. 2011; 2011: 1– 5. https://doi.org/10.1155/2011/743827
25. Sinclair MD. A review of the physiological effects of α_2-agonists related to the clinical use of medetomidine in small animal practice. *Can Vet J*. 2003; 44: 885– 97.
26. LeBlanc MM, Hubbel JAE, Smith HC. The effects of xylazine hydrochloride on intrauterine pressure in the cow. *Theriogenology*. 1984; 21: 681- 90. https://doi.org/10.1016/0093-691X(84)90014-1
27. Gibbs HM III, Troedsson MHT. Effect of acepromazine, detomidine, and xylazine on myometrial activity in the mare. *Biol Reprod*. 1995; 52: 489- 93. https://doi.org/10.1093/biolreprod/52.monograph_series1.489
28. Kindhahl H, Kornmatitsuk B, Königsson K, *et al*. Endocrine changes in late bovine pregnancy with special emphasis on fetal well-being. *Domest Anim Endocrinol*. 2002; 23: 321- 8. https://doi.org/10.1016/S0739-7240(02)00167-4
29. Craft JB Jr, Coaldrake LA, Yonekura ML, *et al*. Ketamine, catecholamines, and uterine tone in pregnant ewes. *Am J Obstet Gynecol*. 1983; 146: 429- 34. https://doi.org/10.1016/0002-9378(83)90823-2
30. Strümper D, Gogarten W, Durieux ME, *et al*. The effects of S+-ketamine and racemic ketamine on uterine blood flow in chronically instrumented pregnant sheep. *Anesth Analg*. 2004; 98: 497– 502. https://doi.org/10.1213/01.ane.0000096243.74182.5e
31. Hartnack AK, Niehaus AJ, Lakritz J, *et al*. Analgesic efficacy of an intravenous constant rate infusion of a morphine-lidocaine-ketamine combination in Holstein calves undergoing umbilical herniorrhaphy. *Am J Vet Res*. 2020; 81: 25– 32. https://doi.org/10.2460/ajvr.81.1.25
32. Anderson DE, Muir WW. Pain management in ruminants. *Vet Clin North Am Equine Pract*. 2005; 21: 19– 31. https://doi.org/10.1016/j.cvfa.2004.12.008
33. Coetzee JF. A review of analgesic compounds used in food animals in the United States. *Vet Clin North Am Equine Pract*. 2013; 29: 11– 28. https://doi.org/10.1016/j.cvfa.2012.11.008
34. Stock ML, Coetzee JF. Clinical pharmacology of analgesic drugs in cattle. *Vet Clin North Am Equine Pract*. 2015; 31: 113- 38. https://doi.org/10.1016/j.cvfa.2014.11.002
35. Kalpravidh M, Lumb WV, Wright M, *et al*. Effects of butorphanol, flunixin, levorphanol, morphine, and xylazine in ponies. *Am J Vet Res*. 1984; 45: 2118- 34.
36. Rialland P, Otis C, de Courval M-L, *et al*. Assessing experimental visceral pain in dairy cattle: A pilot, prospective, blinded, randomized, and controlled study focusing on spinal pain proteomics. *J Dairy Sci*. 2014; 97: 2118– 34. https://doi.org/10.3168/jds.2013-7142
37. Mahen PJ, Williams HJ, Smith RF, *et al*. Effect of blood ionised calcium concentration at calving on fertility outcomes in dairy cattle. *Vet Rec*. 2018; 183: 263. https://doi.org/10.1136/vr.104932
38. Aguilera IM, Vaughan RS. Calcium and the anaesthetist. *Anaesthesia*. 2011; 55: 779- 90.