New Concepts in Bovine Anesthesia

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Introduction

The importance of inducing anesthesia and analgesia to ensure the humane treatment of cattle destined to undergo surgical procedure has been overlooked by some members of the veterinary profession. The reasons for this appear to be diverse. Many of the new anesthetic techniques developed for use in cattle are a result of knowledge gained in applied research. These techniques are not easily implemented under field conditions and, if so, are often costly for the producer. Secondly, relatively few anesthetics or analgesics have been approved for use in cattle by the Federal Drug Administration (FDA). This inability to pass a costly federal regulation process has led to an observed lack of interest by pharmaceutical companies to pursue new anesthetic agents for use in food-producing animals. While prevention of food contamination or adulteration is a desired high priority by the public, FDA regulations pertaining to the use of anesthetics in cattle may be too stringent.[1] Thirdly, the more docile, nonexplosive nature of most cattle when being restrained has led to widespread use of mechanical restraint without inducing anesthesia or even analgesia when handling large numbers of animals. In general, this method of restraint is associated with remarkably little injury to both animal and handler and, thus, remains popular with busy large animal practitioners. The ability to effectively mechanically restrain cattle has also had a significant influence upon the direction of investigation into new anesthetic/analgesic techniques for the bovine species by veterinary anesthesiologists and other investigators. Because of this fact, many new regional and local analgesic techniques have been recommended by anesthesiologists whenever possible in our veterinary teaching hospitals. Similarly, because of the acceptance of mechanical restraint as standard procedure in the field, it appears that the bovine species and indirectly the bovine practitioner have been targeted by some investigators as a good species and willing participants in the assessment and eventual approval of such new anesthetic concepts as electroanesthesia and acupuncture.

Conventional Anesthetic Techniques

General anesthesia of cattle resulting in recumbency for long periods of time (1-2 hr) is often accompanied by severe derangements in cardiopulmonary function. In general, ruminants are even more severely compromised by drug-induced general anesthesia than is the equine. Problems associated with large or small ruminant anesthesia are regurgitation and aspiration of rumenal contents, bloat, hypoventilation and concomitant respiratory acidosis, reduction in cardiac output, tissue hypoxia, and metabolic acidosis.[1] [2] [3] The prevention and treatment of these conditions associated with ruminant general anesthesia have been recently reviewed by Thurmon,[1] Trim,[2] and Weaver.[3]

To achieve sedation or tranquilization of cattle, a wide array of agents and combinations of agents have been utilized. The use of the phenothiazine-type agents such as chlorpromazine (Thorazine),[a] promazine (Sparine),[b] acetylpromazine (Acepromizine),[c] and propriopromazine (Tran-Vet)[d] has largely been replaced by sedation of cattle with xylazine (Rompun).[e] In addition, chloral hydrate has been safely used as a sedative-hypnotic in cattle but, because of its small safety margin, cannot be recommended for induction and maintenance of anesthesia. The induction of general anesthesia in cattle is most often achieved by the administration of a mixture of a barbiturate (thiamylal [surital] or thiopental [pentothal]) and 5% glyceryl guaiacolate (GG) given to effect. An alternative method has been to induce anesthesia with high-dose xylazine administration (0.1 mg/lb, IM). Xylazine has been combined with ketamine to induce 30 min of anesthesia in calves. Xylazine is given at 0.1 mg/lb IM, followed by 5 to 6 mg/lb ketamine IV.[4] Cardiopulmonary derangements have been noted with this injectable technique, as has the maintenance of general anesthesia with the inhalation agents.[5] Inhalation anesthesia for cattle is expensive, requiring the acquisition of a large animal anesthetic machine and a large tilt table for restraining and positioning the animal. For this reason, general anesthesia in most veterinary practices is achieved by using injectable agents or

[a] Pitman Moore Co.

[b] Wyeth Labs

[c] Ayerst Labs

[d] Diamond Labs

[e] Haver-Lockhart Labs

mixtures. Xylazine has become a popular agent for maintenance of short-term anesthesia, with the addition of mechanical restraint. Glyceryl guaiacolate and barbiturate mixtures can also be used for the induction and maintenance of short-term anesthesia of cattle.

Most recently a new mixture of xylazine, ketamine, and GG has been developed and tested for use in cattle at the University of Illinois teaching hospital. This drug combination was initially developed for use in swine and consisted of 500 mg of xylazine and 500 mg of ketamine mixed with 500 ml of 5% GG. This mixture was termed the "triple 500 mixture." Subsequently, the administration of this mixture in other species as a continual infusion appeared promising as well. Because the bovine species is most sensitive to xylazine, the dosage of xylazine was decreased by a factor of 10 when the mixture was made for administration to cattle or calves. Therefore, the bovine mixture contains only 50 mg of xylazine in combination with 500 mg of ketamine in 500 ml of 5% GG. This combination has proven to be very safe and effective for both induction and maintenance of anesthesia in calves and adult cattle.[5] The routine induction dose is ¼ to ½ ml of the mixture per pound. Maintenance of anesthesia can be accomplished with a continual infusion at a rate of approximately ½ ml/lb/hr. The total dose of xylazine and ketamine given IV in this mixture during a 2-hr procedure is less than the required IM dose of these drugs to achieve a comparable period of anesthesia. Perhaps for this reason, recovery from anesthesia maintained with this mixture is remarkably fast and free of complications even after 2 or 3 hrs of surgery. Large bulls have not been anesthetized with this mixture in our clinic. As is the case for most anesthetic agents, neither zylazine nor ketamine has been approved for use in cattle by the FDA.

The advantage of utilizing zylazine as a primary component of an anesthetic mixture is that its actions can be antagonized with appropriate antagonsists. Pharmacologic reversal of xylazine with alpha 2 antagonists such as yohimbine and tolazoline (a mixed antagonist; $alpha_1$ and $alpha_2$) appears to be safe and effective in a variety of species, including the bovine.[5,6] In a recent study by Guard and Schwark,[7] assessment of yohimbine reversal of xylazine sedation was performed in calves. Their results indicated that a 0.25 mg/kg IV dose of yohimbine given 3 min after xylazine administration did not significantly affect xylazine (0.05 mg/kg IV) sedation but did decrease the duration of rumen amotility and reversed xylazine's bradycardic actions. This suggests that appropriate doses of yohimbine may reverse the unwanted side effects of xylazine-induced sedation of cattle.[7] The inadvertent overdose of xylazine or any other alpha 2 agonist appears to be completely reversible with these antagonistic agents. The agent 4-amino-pyridine has been combined with yohimbine as well, to reverse CNS depression of cattle.[6]

Detomidine (Domosedan) is a relatively new alpha 2 agonist with similar physiologic actions as xylazine. It is extremely potent, and it is expected that only minute doses will be required to induce potent and long-lasting effects in cattle. This agent has proven to be safe in the horse producing approximately 2 to 3 times the duration of action as xylazine when given in comparable sedative dosages. At this time, the use of detomidine in cattle is purely experimental.

New Anesthetic Techniques

Although relatively little progress has been made with the chemical restraint of cattle, 2 new concepts have been advanced or reintroduced in recent years to implement restraint, anesthesia, and analgesia of the bovine. These techniques are termed "electroanesthesia" and "electro-acupuncture anesthesia."

The use of electroanesthesia, or perhaps more correctly termed electroimmobilization, is a relatively new concept in the United States. This technique has been advocated for restraint of cattle while performing minor surgical procedures. Originally, this technique was explored and developed by investigators working with the Australian government in order to assess the feasibility of electrically induced restraint for robotic sheering of sheep.

In a recent study, Kuckel et al.[8] assessed the cardiovascular physiologic effects of 30 min of continual electroimmobilization in sheep. It was concluded that severe cardiopulmonary effects did not occur during the period and that a rapid return to baseline cardiovascular function followed termination of stimulus. It was concluded that this technique did not appear to be life-threatening.[8] Other studies have emphasized the achievement of immobilization without accomplishing the major requirements for anesthesia (i.e., muscle relaxation, analgesia, and unconsciousness).[9,10] Unconsciousness is usually assessed as adequate in man if amnesia and inability to recall the surgical experience is achieved. Work completed by Grandin et al.[9] in sheep has convincingly demonstrated the recall of an electroimmobilizing episode indicating the inability of this technique to achieve this major action of anesthesia. Results from this study did not indicate an indifference to this technique but rather a strong negative behavioral response.[9] This technique appears aversive in nature and indeed may have induced significant pain, which is, of course, inconsistent with the definition of anesthesia.[10] Assessment of electroanesthesia for dehorning of cattle has also been recently reported.[11] Results from this trial indicated that the application of an electroimmobilizing stimulus may be painful and should not be considered as capable of inducing analgesia. The difficulties of assessing pain when an animal is immobilized with electrical stimulus are obvious and should be recognized by investigators.

In conclusion, there is always an appeal for quick methods of restraint when large numbers of cattle are being processed, but the benefits may be outweighed by the adverse effects upon individual animals. In the absence of evidence that

commercial immobilizers do not induce the major components of anesthesia and may, in fact, induce a degree of pain and discomfort, it should be emphasized that immobilization by an unpleasant technique to perform a known painful procedure is adding insult to injury. This may work against our efforts as a profession to create a positive animal welfare image. If painful procedures must be performed, as is often the case in processing large numbers of cattle, the masking of this pain with immobilizing techniques provides no advantage and may be perceived as attempts to deceive producers and the public in general.

In contrast to the questionable results observed with electroimmobilization techniques, data showing the effectiveness of acupuncture techniques in achieving analgesia and even anesthesia in the bovine are more positive. Acupuncture techniques are numerous, including aquapuncture (e.g., injection of vitamins at specific sites), sonopuncture (ultrasound points), cryoacupuncture (freeze points), acupressure (pressure points), laser-puncture (laser points), and electroacupuncture (electrical stimulation of precisely placed needles). The advantages advanced for acupuncture over local analgesia achieved with chemicals are the ability to extend effect indefinitely, the absence of toxic reactions (central or local), and the inexpensive administration after initial investment. A disadvantage is the time required to develop new skills and techniques, and achievement of the desired analgesic effect may be very time-consuming. A variety of acupuncture techniques have been tried in treating a plethora of diseases and conditions. Induction of parturition and estrus, treatment of mastitis, lameness, indigestion, and tetanus have all been reported to be successfully treated with the help of acupuncture.[12] White et al.[13] have recently reported that electroacupuncture can be used to successfully induce analgesia in the paralumbar fossa of the cow. Good analgesia was achieved suitable for abdominal surgery in standing cattle.[13] Some sedation was also noted by these investigators. Sedation and analgesic actions induced by electroacupuncture are likely the result of release or production of endogenous opiate-like substances (endorphins and enkephalins) within the CNS, since an increase in these substances are noted with acupuncture needle stimulation at an appropriate electrical frequency. Thus the use of electroacupuncture for regional analgesia may be a legitimate alternative to local analgesia and regional nerve blocks with local analgesic agents.

The induction of general anesthesia in cattle and horses with electroacupuncture techniques has been attempted.[12] Acupuncture experts point out that the successful induction of anesthesia via electroacupuncture requires precise placement of needles along the passage of major nerve trunks or so-called "anesthetic lines." Continuous electrical stimulation is necessary to maintain excitation of CNS and damping or suppression of painful stimuli.[12] Overstimulation of these "anesthetic lines" may actually lead to a hyperalgesic effect. Therefore, a suitable intensity of stimulation must be found. The stimulation of peripheral nerves in itself does not induce anethesia but rather stimulation of an intact CNS receiving information from peripheral nerve stimulation is required to induce anesthesia. The radial, median, seventh cranial, and pelvic nerves have all been successfully utilized as "anesthetic lines" to induce a state of equipotent anesthesia in large animals.[12] In contrast to electroimmobilization, an appropriate stimulation via accurately inserted needles along major nerve trunks (anesthetic lines) advocated by acupuncturists to induce general anesthesia may be an effective alternative to the chemical restraint techniques presently utilized in western medicine, human and veterinary.

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Questions & Answers:

Question:

Answer: Butorphanal is interesting. It's a so-called agonist antagonist. There are three agonist antagonist narcotics that we have available to us now. And they are good because you don't need a narcotic license. The only problem is that when you read the label, it will say five times as potent as morphine. And that's really not quite true. Everybody has a tendency to think that you can use butorphanal and you're going to get a more profound analgesia with butorphanal than you do with morphine. And that's not true at all. In fact, everybody that uses a drug like butorphenol to try and produce potent analgesic effects for post-op pain, are unhappy in general, because they don't get the analgesia that they would with morphine. That's a real complicated thing be-

cause you have to talk about affinity and intrinsic activity and ceiling effects and all such things as that. But I know if you combine with xylazine it is very good in the horse. We've used it in dogs. It has an antitussive effect. But in cattle I'm not sure butorphanal has ever been used in cattle.

Question: What is the standard dose of yohimbine for reversal of xylazine?

Answer: It's .125 mgs per kg, .06 or so per lb. It's pretty standard for all the species. So there are not a lot of new concepts. I think the idea of going to continual infusion with a mixture like this and for a long period of time and not seeing a lot of cardiovascular depression is new and usable. For induction a lot of people will use something like a tenth of a mg per lb. IM with xylazine. Wait five minutes or so and come back, 5 mgs or so per lb. IV or IM with ketamine. That will get induction of anesthesia and a lot of people re-administered those two drugs just as injectables to produce anesthesia for a period of time, half a dose at a time. In our junior surgery labs that's what we are doing. We're using goats and we give them xylazine and ketamine with one lab and of course they sit there and they say we need more and we give them a little more xylazine and that's not good, give them a little bit more ketamine. And what you find out is if you've got an animal that is rigid acting you give more xylazine. If you have an animal that's reacting to pain you end up giving maybe a little bit more ketamine and xylazine together. It's more of an art than a science.

Question: Have you tried it on bulls?

Answer: We have not. All the bulls we get are client animals and we just have not had the guts to do it yet. But it probably is going to work. The only thing is that certain breeds like Charolais are supposed to be extremely susceptible to xylazine. To administer that IV the way we do, I don't know what would happen.

Question: What is the dosage?

Answer: 5-6 mgs per lb. There have been several papers on xylazine-ketamine combinations for calves and for adult cattle for induction of anesthesia and for maintenance of anesthesia. It's a viable combination.

Question: Do you have a dose rate for cattle?

Answer: No, I really don't have a dose rate in cattle. I'm not . . . no, people just administer it in ccs to effect. And, of course, it has this tremendous margin of safety so you can give huge doses and just get maybe a prolonged period of stimulation. But there's a point to be made about using doxapram hydrochloride (Dopram) versus yohimbine. Doxapram produces a physiologic reversal versus pharmacologic reversal. In other words, if you work at the same receptor site, yohimbine is working at the same, exact membrane receptor site as xylazine. So that you're getting true pharmacologic reversal and you will not see the animal fall back into sedation. That's not the case with doxapram. You give doxapram, you may stimulate an animal for a period of time and that effect wears off and he will fall back into sedation because the xylazine is still there. unless the xylazine is metabolized away. So actually yohimbine is better for reversal than doxapram. But if doxapram is all you have it is all right. In the case of that cow where we gave 3 ccs, yes, we gave doxapram and the cow was sort of awakened. And the next time we drove by she would be down again. But if we had yohimbine she would get up and stay up.

Question: What are some of the surgical operations you have performed using these products?

Answer: In sows, caesarean sections. Lots of laparotomy type procedures, reproductive procedures of all sorts. I believe we have done one bone plating where we had to run in lots of it and we were worried what was going to happen. We got through all right.