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Anaesthetic solutions for the castration of newborn piglets
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Castration is a documented painful surgical intervention in newborn piglets and should ethically and lawfully (in some countries) be performed under anaesthesia. Castration is performed to increase meat quality by preventing boar taint, avoid indiscriminate breeding and maintain general control of stock. Alternatives to surgical castration are being explored including immunocastration and genetic manipulations.

What is pain?
The International Association for the Study of Pain (ISAP) has defined pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage". They also remarked that "the inability to communicate in no way negates the possibility that an individual is experiencing pain or is in need of appropriate pain-relieving treatment".
As early as the 17th century it was proposed by Descartes in his "Traite de l'homme" (1664) that pain was transmitted by a string from the site of the noxious stimulus to the pineal gland, which was considered the "conscious centre". This is very similar to our modern definition of nociception. Nociception is a motor response designed to remove tissue from potentially damaging insults and involves the transduction, transmission and modulation of neural signals from the site of the stimulus to the central nervous system (Lamont et al. 2000).
Often though (as with a surgical insult or injury) the pain is associated with tissue damage and inflammation, which leads to hyperalgesia and pathologic pain due to infiltration of the injured tissue with inflammatory mediators. This inflammation makes the tissue more sensitive in order to protect the site of injury from further damage.

Do animals experience pain?
Rene Descartes (1596-1650) remarked that "animals cannot talk, therefore they cannot think and therefore they cannot feel pain." Unfortunately this line of thought is still present today. But "the question is not can they reason? Nor can they talk? But can they suffer?" (Jeremy Bentham 1748-1832). We now have significant evidence from the study of anatomy, physiology and behaviour to conclude that they do.

Is castration painful and how can we assess this pain?
The Federation of European Laboratory Animal Science Associations has listed testes as one of the most sensitive tissues to pain. Wemelsfelder and van Putten (1985) observed that castrated piglets had increased lying times post-castration compared to their female littermates. McGlone et al. (1993) also showed that 1,5,10,15 and 20-day-old castrated piglets had reduced suckling, reduced standing and increased lying times compared to their intact male littermates. White et al. (1995) observed that piglets vocalize more if they are castrated than if they are similarly handled and not castrated. Taylor et al. (2000) determined that the cutting of the spermatic cord was the most painful part of the castration, as this part of the procedure evoked the greatest amount of calling.

Surgical castration has also been shown to induce an endocrine response (Prunier et al., 2005). Increased ACTH, cortisol and lactate levels were found in castrated piglets when compared to sham-castrated piglets. Tooth resection and tail docking did not induce a similar endocrine response in this study.

Why treat the pain?

"The greatness of a nation and its moral progress can be judged by the way its animals are treated" (Mahatma Gandhi).

There are moral, ethical and other reasons why pain should be treated. Medically speaking, pain is correlated with stress. Pain induces a sympathetic and catabolic response with effects such as an increase in myocardial work and oxygen consumption. With prolonged exposure, these effects can be detrimental. Remarkably, as late as the 1980s, human neonates were experiencing major cardiac surgery without adequate pain control. The reasons for this included lack of approved drugs for use and lack of knowledge of their side effects in such young patients. In a study performed at Children's Hospital in Boston, MA (Anand and Hickey, 1993) it was found that use of deep anaesthesia with sufentanil, a potent opioid, resulted in significantly lower morbidity and mortality when compared to a lighter anaesthesia with halothane and morphine proving that the side effects of inadequately controlled pain were severe. Other reasons to treat the pain include the increased awareness of the public to animal pain, consumer satisfaction and laws in countries such as Norway and Switzerland which prohibit castration without anaesthesia and pain control.

How can we treat the pain?

Pain can be treated at three different levels. Drugs can be administered that block the transmission of pain to the spinal cord (treatment at the site of injury); they can work at the site of transduction (spinal cord level) or can alter modulation or awareness (central nervous system). In a landmark discussion on pain physiology, Woolf and Chong (1993) showed that the hypersensitivity reaction that accompanies tissue damage could be prevented by treating the pain before it occurs (pre-emptive analgesia).

What has been studied on anaesthesia specifically for castration?

The ideal anaesthesia for piglet castration would be short acting, inexpensive, safe with minimal cardio-respiratory side effects, be easy to administer and approved for use in swine.

1. Local anaesthesia: The current practise in Norway is to use local anaesthesia. Arguments against this technique have included that the pain of the injection was as bad or worse than the castration itself. In a study by Haga and Ranheim (2005) piglets were anaesthetized with halothane and sympathetic responses to the injection of the local aesthetic and the castration itself were compared. It was found that the blood pressure and pulse rate responses to castration without local anaesthesia were significantly larger than the response to the lidocaine injection. Ranheim et al. (2006) also studied the distribution of radiolabelled local anaesthetic when injected directly into the testes. The lidocaine diffuses readily from the testes through the spermatic cord but not through the tunica vaginalis into the cremastor muscle explaining why nociceptive response may still be present during castration with local anaesthesia. Advantages of local anaesthesia are that general anaesthesia is not required, an analgesic effect is present and only one drug is needed. Disadvantages include incomplete spread of local anaesthetic and that the animal must be handled twice as the drug needs time to take effect.
2. Injection anaesthesia:
   In 1994, Waldmann et al., did a comparison study of several different injectable agents including tiletamin/zolazepam, thiopentone and propofol in piglets four to thirteen days of age. They demonstrated that

tiletamin/zolazepam (10 $mg \cdot kg^{-1}$) intramuscularly and propofol intraabdominally (4 $mg \cdot kg^{-1}$) did not produce enough relaxation and anaesthetic depth and piglets experienced a long and difficult recovery. Thiopentone intraabdominally (30 $mg \cdot kg^{-1}$) produced good anaesthesia but the death rate was 9.5% due to crushing of the piglet by the sow. McGlone et al. (1993) studied the effect of the combination of ketamine, xylazine and guafenesin given intravenously in two and seven week old piglets. The death rate of the two-week-old animals was very high (five of eighteen animals) and the recovery period of the surviving animals was very long.
In the study by Kmiec (2005), a dose combination of 2 $mg \cdot kg^{-1}$ azaperone and 25 $mg \cdot kg^{-1}$ ketamine IM was found to be most effective in the initial trial, which compared six different dose regimens. Recovery time in the 2 $mg \cdot kg^{-1}$ azaperone 25 $mg \cdot kg^{-1}$ ketamine group ranged between 198 and 234 minutes. Advantages of injectable anaesthesia include post-operative analgesia, easy administration, and minimal equipment. Disadvantages include that the animal needs to be handled twice, there is no dosing "to effect", there is no single drug available for optimal anaesthesia and drugs have abuse potential for humans.

3. Inhalation anaesthesia:
Several different gases have been studied. Carbon dioxide (CO2), applied in different concentrations with oxygen was studied by Lauer (1994), Körte (1996), Kohler et al. (1998) , Steenblock (2002) and Thurmon et al.(1991). The authors describe a very fast induction and a complete analgesia for a short intervention together with a fast recovery. Unwanted side effects consisted of hyperventilation and agitation during induction and gasping during castration. These findings, together with increased stress hormone levels, have made this method questionable. (Kohler et al., 1998).

Inhalation of 5% halothane applied by a simple mask in oxygen through a simple breathing system induced anaesthesia within two minutes. Together with an uneventful recovery, the method seemed to fulfil the main requirements for a pain free castration. In a field study evaluating time and costs, the method has proven suitable for routine castration of piglets less than two weeks of age (Wenger et al., 2002). Concerns were expressed by the pork industry against the technique because of the health hazards to exposed personnel. Halothane has been since withdrawn from the European market.

Isoflurane was then looked at in a study comparing isoflurane (iso) and isoflurane/N20 (iso/N20) in 85 piglets. This method was shown to be fast, safe and practical. The study included involvement of the Swiss Office of Secure Working Environments (SECO) and a special mask was developed. It consisted of a double mask, applying the anaesthetic gas in the inner mask with any leaks scavenged by means of a pump. Pollution could thus be reduced to a minimum. The mask was also equipped with a valve to allow gas flow only when in contact with the animal's snout. Induction of anaesthesia proved to be smooth and the palpebral reflex disappeared within 36.5 seconds in the iso/N20 group and within 51 seconds in the iso group. Anaesthesia and analgesia were sufficient (mean total anaesthesia time 128 (30-390) seconds) in the iso group. No deaths occurred (Walker, 2002)

Another method of delivering isoflurane was developed using a portable inhaler (Hodgson, 2006). Induction occurred within 47 seconds and recovery time was less than two minutes. Only a small number of animals were studied but the author described effective anaesthesia for castration. The main disadvantages with this device are that liquid isoflurane has to be drawn

up and applied into the device separately for each piglet and adequate scavenging is not present. Further study and development is needed before this device can be accepted.

Advantages of inhalation anaesthesia include easy control of the depth of anaesthesia, anaesthesia can be dosed "to effect", there are fast induction and recovery times and very little tissue residue is present. Disadvantages include the need for a bulky apparatus, post-operative analgesia is not present and environmental pollution needs to be controlled.

4. Intranasal anaesthesia:

A comparison of intranasal and intramuscular application of a ketamine, climazolam and azaperone combination was recently looked at by our institution (Axiak et al., unpublished results). Intranasal anaesthesia was associated with a more unpredictable level of anaesthesia, which consistently became worse as the ambient temperature became colder. Intramuscular application provided a more consistent and reliable anaesthesia but had significantly longer although acceptable recovery times (median 80.5 minutes (95% confidence interval 66;132)). Intramuscular application of this combination could prove to be a suitable alternative for piglet castration but the major disadvantages of this technique are that benzodiazepines, such as climazolam, are not approved for use in swine, climazolam is being withdrawn from the Swiss market and the benzodiazepines need to be antagonized to have acceptable recovery times. Currently, further work is in progress at our institution looking at other benzodiazepines to replace climazolam and studying intranasal application under controlled environmental conditions.

Does anaesthesia have a role for piglet castration?

Further study is needed, but isoflurane in combination with a suitable analgesic such as meloxicam; lidocaine by local injection; and the ketamine, azaperone and climazolam combination all present reasonable solutions and provide both anaesthesia and analgesia with a short recovery. Unfortunately, all have their own unique disadvantages that must be considered.

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