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Review article

Chemical sterilisation of animals: A review of the use of zinc- and $CaCl_2$ based solutions in male and female animals and factors likely to improve responses to treatment

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ABSTRACT

Chemical sterilisation can be used as an alternative to surgical castration in some circumstances. This review focuses on responses to treatment with zinc- or $CaCl_2$-based chemosterilants, factors that have affected treatments and their potential use to sterilise female cattle. Successful treatment with a low incidence of adverse side effects in male animals has occurred with the use of zinc gluconate (ZG), neutralised in arginine and a 20% solution of $CaCl_2$ in ethanol. Injection technique plays an important role in success. Less satisfactory results appear to occur following use in animals with relatively larger testes. In animals with relatively small testes adjustment of the dose according to testicular size appears to optimise results. The techniques appear to be most suited to population control strategies in companion animals where low cost treatment of animals in environments where surgical facilities and specialised aftercare are lacking. The need for careful administration and likely slower speed of administration compared to surgical castration are likely to hamper application within the cattle industries. Recently transvaginal, intraovarian administration of $CaCl_2$ in ethanol has been shown to cause complete ovarian atrophy without apparent pain in some heifers, although variable responses were found. Chemical sterilisation can play a role in the sterilisation of animals but careful attention to dose, volume, chemical composition, administration technique are needed to avoid adverse side effects and variability in responses associated with some treatments. Application in female animals requires further study but $CaCl_2$ in ethanol can potentially cause complete ovarian atrophy when administered to heifers.

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1. Introduction

Sterilisation of animals dates back to 7000–6000 BC with professional oversight of the practise being documented from the 15th to the 19th centuries (Purswell and Jöchle, 2010). Sterilisation of domestic animals is used as a means of controlling animal numbers, improving genetic gain by restricting gene transfer to genetically elite animals, modifying animal behaviour and altering carcass composition in animals that are used as sources of food for human consumption. The ideal sterilisation technique would enable sterilisation of animals with a single, permanent, low cost treatment that does not have a negative impact on animal welfare and productivity. It would be easy to administer and be specific for the animal being treated without affecting non-targeted individuals within the same or other species. In males and females it would also have a consistent effect in suppressing gametogenesis and on moderating behaviour by suppressing or abolishing the synthesis of steroids that influence behaviour (Jana and Samanta, 2011). In the case of animals that are used for human consumption it would also not leave any unacceptable tissue residues and be acceptable to consumers.

A variety of methods have been used to sterilise animals including the use of hormonal inhibitors of ovulation such as synthetic progestins (melengestrol acetate, levonorgestrel), GnRH agonists such as deslorelin, contraceptive vaccines which inactivate GnRH and prevent ovulation or spermatogenesis and vaccines that target the zona pellucida and prevent sperm binding and fertilisation (Massei and Miller, 2013). Newer developments have included the development of recombinant viruses that express antigens and toxin conjugates that destroy gonadotrophs (Massei and Miller, 2013). Chemosterilants are chemical agents that when administered directly to an animal affect gamete and/or gonadal hormone synthesis and/or prevent the transport of gametes. In males chemosterilants that prevent spermatogenesis or result in ductile occlusion preventing outflow of sperm have been widely studied (Bowen, 2008; Massei and Miller, 2013) but studies aimed at directly suppressing ovarian function or gamete transport in females are lacking. Variations in responses to chemosterilants have also been obtained in different studies. The aim of this review is to assess responses to two of the most commonly used chemosterilants, zinc and $CaCl_2$ based chemicals, in male and female animals and to identify factors that have contributed to variability in responses to treatments.

2. Circumstances that favour the use of chemosterilants

Use of chemosterilants has been favoured where culling of animals may be undesirable for religious or cultural reasons and where purpose built facilities to perform surgical sterilisation are lacking. Chemical sterilisation offers the advantages of a single, low-cost and permanent treatment without the need to return to administer boosters or repeat treatments. It also may be useful where cutaneous myiasis can complicate surgical treatments. It can also avoid other potential adverse outcomes of surgery that include haemorrhage and herniation (Jana and Samanta, 2007). Often no or only light sedation is required, pre-surgical preparation is minimal and postoperative care is in most cases is not required. For these reasons chemical sterilisation, in some species, also offers a means of sterilising large numbers of animals in short periods of time, allowing animals to be returned rapidly to the community without the need for follow-up care. As such this technique has become favoured in regions where financial capacity and the availability of surgical resources and surgically trained personnel may be limiting capacity for population control (Esquivel Lacroix, 2006; Levy et al., 2008). Combining a zinc-based chemosterilant with rabies vaccine has also been attempted to enable simultaneous castration and vaccination of dogs (Wang 2014). In agricultural animals community concerns surrounding the welfare of surgical castration persist (Petherick, 2006). Development of alternative methods of castration which are not adverse to animal welfare could also be more acceptable to consumers.

3. Substances used as chemosterilants

A variety of chemical substances have been used as chemosterilants. Some examples include, cadmium (Chatterjee and Kar, 1969; Patra and Bose, 1990), calcium chloride (Jana et al., 2005a; Jana and Samanta, 2007), chlorhexidine, formalin, methalibure (ICI-33828), dexamethasone, metoprion (SU-4885, Ciba), niradazole (33644-Ba, Ciba) a- chlorohydrin (U-5897), Bacillus Calmette Guerin (BCG) (Kutzler and Wood, 2006), danazol (Dixit et al., 1975), zinc tannate (Migally and Fahim, 1984), lactic acid (Fordyce et al., 1989), ethanol (Raman et al., 1976), silver nitrate, acetic acid, formaldehyde, sodium tetradecyl sulfate (Freeman and Coffey, 1973), α-hydroxypropionic acid (Cohen et al., 1990), glycerol (Wiebe et al., 1989; Immegart and Threlfall, 2000) and microbial extracts (Roy et al., 2017). Treatment with chemosterilants in males, in some studies has resulted in side effects such as pain, incomplete responses to treatment, persistence of male-like behaviour and suppurating scrotal fistulae. Some chemicals, such as cadmium or formalin would also not be acceptable for use in food producing animals due to likely concerns of consumers and regulatory agencies (ATSDR, 2017). Fordyce et al. (1989) also commented that chemical castration of calves weighing <128 kg, with lactic acid, took three times longer than surgical castration, pain responses persisted for up to 3 days in some calves while the technique may require more skill than surgical castration. Cohen et al. (1990) commented that chemical sterilisation when applied to male calves requires more