Online Journal of Animal and Feed Research

Volume 9, Issue 6: 233-240; November 25, 2019



Received: May 06, Revised: November 15,

,2019

, 2019

PII: S222877011900032-9

REVIEW

ARTICLE

DOI: https://dx.doi.org/10.36380/scil.2019.ojafr32

REVIEW ON CHEMICAL CASTRATION METHODS Α ΤO CONTROL STRAY DOG POPULATION

Dr. Addisu Mohammed SEID and Demr Abebe TEREFE

University of Gondar College of Veterinary Medicine and Animal Sciences, Gondar, Ethiopia

Email: addisvet838@gmail.com; ORCID: 0000-0002-5546-2857

Supporting Information

ABSTRACT: About 75% of dogs worldwide are free to roam and reproduce, thus creating locally overabundant populations. Problems caused by roaming dogs include diseases transmission to livestock and humans, predation on livestock, attacks on humans, road traffic accidents, and nuisance behavior. Nonsurgical fertility control is increasingly advocated as more cost-effective than surgical sterilization to manage dog populations and their impact. The aim of this review was to illustrate the spectrum of fertility inhibitors available for dogs. Although surgery is the most effective and safe procedure, it is also expensive to use of non-surgical, sterilization methods that would make male sterilization inexpensive, easy and fast for sterilization of large number of male dogs within short period of time to effectively contribute in curbing the growth of the stray dog population were introduced. Chemical sterilization methods so far employed included hormonal methods, immunocontraceptives and inorganic chemo-sterilants (chemo-sterilants such as CaCl₂, zinc gluconate neutralized by arginine (Neutersol) and hypertonic sodium chloride-NaCl solution. Intratesticular injection of calcium chloride, Zinc gluconate and 20% NaCl hypertonic solution showed a promising result as chemical sterilants. The review concluded that the main challenges for the future are evaluating the feasibility, effectiveness, sustainability, and effects of mass non-surgical sterilization campaigns on dog population size and impact as well as integrating nonsurgical fertility control with disease vaccination and public education programs. The review also showed the relative lack of research or knowledge related to fertility inhibitors in developing country as Ethiopia and suggested that more works is required in this country.

Keywords: Chemical sterilization, Dog population management, Fertility inhibitors, Stray Dogs.

INTRODUCTION

Dogs are one of the primitive companion animals to be domesticated by man. Their domestication dated as far back as 8,000 BC (Matznick-Koler, 2002). Street dogs are common in the developing world, and often live with little or no veterinary care, consuming refuse and feces to survive. The uncontrolled growth of a dog population can have a negative impact on public health and can create socioeconomic, political, and animal welfare problems (OIE, 2016). The global dog population is estimated to be around 700 million (Hughes and Macdonald, 2013). Problems caused by free-roaming dogs include diseases transmitted to livestock and humans, predation on livestock, bites, road traffic accidents, and nuisance such as barking and soiling of parks and recreational areas (Macpherson et al., 2013).

Domestic dogs are successful breeders in almost all kinds of environments, but are always directly or indirectly dependent on man. Since their domestication more than 14 thousand years ago a strong link between dogs and humans has been established. Nowadays that link persists even stronger, since the affection for and loving care given to this species has generated a tremendous industry devoted to caring for its health, nutrition, training, etc. However, as a consequence of uncontrolled reproduction, overpopulation of this species (probably the most abundant carnivore species on earth) has become a big concern in many countries where stray and feral dogs are causing zoonotic diseases, nuisance, pollution of parks and recreation areas, damage to livestock and destruction of ecosystems. In addition, the relinquishing of dogs to animal shelters incurs great costs for the maintenance or euthanasia of dogs because not enough households are available for their re-homing (FAO, 2014).

Dogs play a number of important roles in human societies: they provide companionship and are used for a variety of activities including hunting, herding other animals and guarding property. Animals live in close contact with human beings. In many countries, however, an increasing number of unwanted, unhealthy and unvaccinated dogs are found roaming. This is especially the case in countries with limited social and economic development as well as in places where civil unrest or armed conflict have forced people to flee from their homes and leave their dogs behind. Abandoned and free-roaming dogs can give rise to a series of human and animal health and welfare concerns, in urban spaces and in other human habitats. The availability of more food waste, due to changes in society such as urbanization and increased human densities, combined with a lack of responsible ownership, are leading to an apparent increase of free-roaming dogs (Pal, 2005).

National and international organizations working on dog population management and welfare often classify dogs in the following categories, according to ownership and degree of confinement: owned and permanently confined within household premises; 2) owned by a single household but free to roam; 3) "community owned," with several households or people providing food and shelter but free to roam; or 4) ownerless and free-roaming. As a consequence of uncontrolled reproduction, canine overpopulation remains a problem facing many countries throughout the world, where it creates locally overabundant populations of animals that are often in poor health and have a high turnover because of low survival rates. Approximately 75% of the global dog population is free roaming or stray dogs, living mostly in Latin America, Africa and Asia (Matter and Daniels, 2000).

The need to control the number of dogs, especially stray dogs, is motivated in part by public health concerns, particularly in relation to rabies transmission. Additionally, echinococcosis/hydatidosis and leishmaniasis are serious zoonotic diseases transmitted by dogs (ICAM, 2007).

There are two techniques for sterilization known as surgical and chemical. Surgical castration removes the testes from the scrotum via an incision in male animals. This method is effective, but infection or bleeding can become a problem and it is also time consuming, not cost-effective and needs skilled surgeons. Moreover, this method is not effective for large-scale application, especially for controlling large population size of undesirable mammals in the community like stray dogs. Besides this, postoperative care and management of the animal are also required to prevent infection (Jana et al., 2007).

The use of inorganic chemo-sterilants in male dogs is an attractive option because it removes the disadvantagesand costs of surgical sterilization and post-operative care (Rojas et al., 2011). Furthermore, in regions where surgical castration of male dogs is not culturally accepted (e.g. Romania, the Bahamas) chemical castration offers a reasonable alternative. Hence, chemical castration could be an attractive option for developing countries with limited resources for surgical dog management programs (Garde et al., 2016). Surgical castration has disadvantages and postoperative complications of surgical methods of sterilization such as hemorrhage, wound dehiscence, infections, and scrotal swellings (Adin, 2011). In order to minimize post-operative complications and costs associated with conventional surgical castration, other in situ noninvasive approaches have been used which include immune-castration and chemical castration (Abshenas et al., 2013).

The use of non-surgical, inexpensive and easy sterilization methods of a large number of male dogs would effectively contribute to curb the growth of the pet population. Alternative methods to surgical sterilization that are effective, easy to administer, safe, and affordable would offer immense benefits, allowing animal welfare organizations, public health programs, and governments to reach further with limited resources (Briggs, 2012). Immunocastration works as a vaccine, stimulating the immune system to produce antibodies against the gonadotropin-releasing hormone (GnRH) (Thompson, 2000). About 99% of rabies deaths occur in developing countries 55% in Asia and 44% in Africa. Rabies mortality ranges from 0.001 per hundred thousand in the United States to 18 per hundred thousand in Ethiopia, with mortality levels of 0.01 in South Africa, 0.47 in Thailand and Vietnam, 0.57 in Sri Lanka, 1.75 in Bangalesh, and 2–4 in India (Haupt, 1999).

The ideal non-surgical castration technique should produce permanent loss of fertility, permanent loss of sexual behaviour including displays of some forms of aggressive behaviour, requires single injection, safe, with no deleterious side effects for the target and non-target species (including humans) in case of accidental exposure or self-injection, has good efficacy (high success rate in treated animals), technically feasible, stable in formulation, allow for storage and handling under field conditions and should be affordable and cost effective (Kutzler and Wood, 2006).

Calcium chloride (CaCl₂), delivered as intratesticular injection, is being researched as a sterilant for dogs. CaCl₂ caused atrophy of the seminiferous tubules and decreased testosterone concentration and sperm count in a dose dependent manner (Jana and Samanta, 2007). The low cost, ease of use, and cultural acceptance of a sterilization method that does not require removal of the testes make male sterilants a valuable tool for large-scale sterilization campaigns, particularly in areas lacking clinical facilities or skilled staff (Levy and Crawford, 2008). Sodium Chloride Solution - Hypertonic saline is a solution that is inexpensive and easy to administrate. Hence, chemical castration could be an attractive option for developing countries with limited resources for surgical dog management programs (Garde et al., 2016).

In Ethiopia Stray dog population spreads several zoonotic diseases majorly rabies. Dog population risk in Ethiopia by rabies the national annual estimates from official reports indicate 12 exposure cases per 100,000 population and 1.6 rabies deaths per 100,000 population (Deressa et al., 2013). However, the actual numbers are expected to be higher as many cases are not reported (Moges, 2015). Rabies is an endemic disease in Ethiopia claiming thousands of lives each year. It is a serious challenge in Tigray region, Northern Ethiopia, both in humans and animals. A report from Tigray Bureau of Health indicates an estimated 4729 dog bite cases and 44 deaths from 2009-2012 in the region (TBOH, 2012).

Therefore the main objectives of this review are: The potential uses of non- surgical castration methods to control stray dog population; to reduce the cost of surgery and complications; and to give updated information about chemical castration other than surgical intervention

LITERATURE REVIEW

Dog classification

Populations of dogs vary between different habitats, different cultures and different social strata of the human populations. In developing countries, a large number of free roaming dogs have owners and are classified according to the

WHO (1990) based on the level of restriction or supervision as family dogs (fully dependent; semi-restricted) which can have access to the streets, and neighborhood dogs (semi-dependent, semi-restricted or unrestricted). The presence and abundance of stray dogs depends on the attitudes towards dogs of the humans in these areas. Stray dogs have a great impact on human public health and the ecosystems. Due to the close contact with humans, dogs are responsible for the spread of several zoonotic diseases. Dog rabies is endemic in many developing counties and is responsible for most human deaths from the disease. In addition, at least 65 other zoonosis including ancylostomiasis, echinococcosis, leptospirosis and salmonellosis, may be transmitted to man by direct contact or contact with secretions and excretions of pets. Additionally, domestic dogs are potentially effective predators of the native fauna and can have competitive interactions with endemic wild carnivores (Butler et al., 2004).

Strategies to control the overpopulation of free-roaming dogs include enforcement of law, education of owners and sterilization of pets. In many developing countries, mass euthanasia of dogs is systematically-used in an effort to reduce the density of free-roaming dogs and prevent the transmission of zoonotic diseases. However, this strategy cannot be effective in the long term without the enforcement of laws and education of people. Free-ranging domestic dogs are non-cooperative populations, i.e. they are not dependent on other animals of the same species to survive. Any reduction in the population density through additional mortality is rapidly compensated by better reproduction and survival. In a hypothetical model adding mortality (a) at different magnitude and frequency to two different kinds of populations, non-cooperators (b) and cooperators (c) shows than non-cooperator breeding populations can recover quickly even from important or frequent perturbations (Courchamp et al., 1999).

The most important canine zoonosis includes rabies, leptospirosis, Chagas disease, echinococcosis, and leishmaniasis (Garde et al., 2013). Rabies is caused by fatal encephalitis in most mammals including humans. Animals like dogs, bats, raccoons, skunks and foxes act as reservoirs and the virus is transmitted through bites and licking. The incubation period can vary between 2 weeks and several years, with an average of 2-3 months (WHO, 2005).

DISCUSSION

Methods of chemical contraception and chemical sterilant

Reproduction control utilizing chemical or immunological methods offers a humane and less expensive alternative to surgical sterilization (FAO, 2014). Contraception in dogs can be achieved through chemical reproductive control, which prevents pregnancy by temporarily or permanently sterilizing these animals (Kutzler and Wood, 2006). Chemical fertility control can be achieved through contraception, which prevents the birth offspring but maintains fertility or by sterilization, which renders animals infertile (Kutzler and Wood, 2006). Chemical sterilization methods so far employed include hormonal methods, immunocontraceptives and Inorganic chemo-sterilants such as CaCl2, zinc gluconate neutralized by arginine (Neutersol), NaCl solution (Kutzler and Wood, 2006).

Hormonal methods. Gonadotropin-releasing hormone (GnRH) is a decapeptide synthesized and stored in GnRH neurons located There have been three isoforms of GnRH recognized in animals; mammalian GnRH-I, chicken GnRH-II, and lamprey GnRH-III (Khan et al., 2007). However, GnRH-I is accepted as the main fertility-regulating peptide (Khan et al., 2007). Release of GnRH is controlled by steroidal hormone feedback as well as non-steroidal hormones, such as melatonin, catecholamines and opioids. GnRH is one target for fertility inhibitors. GnRH controls the release of the pituitary gonadotropins, Follicle stimulating hormone (FSH) and Luteinizing hormone (LH), which in turn control the production of sex hormones and ultimately ovulation, spermatogenesis, and sexual behavior (Massei and Miller, 2013). The working mechanism of these agents consists in binding to GnRH receptors and therefore stopping the action of endogenous GnRH. This suppresses gonadotropins secretion and blocks the ovulation without initial stimulatory effect. When given to pregnant bitches it can induce abortion which is not the case in queen. In 2006 an implant containing nafarelin at a dose of 18.5 mg, called Gonazon, was introduced on the European market. This compound is inserted in the umbilical region in dogs, and in the neck in cats (Gobello, 2012). Another formulation of GnRH agonist is marketed as the implant Suprelorin comprising of a GnRH analogue, named deslorelin. Its activity is similar to what is described above, but currently it is only registered for temporary chemical castration of male dogs. Off-label use has shown that the drug can also be used for long-term prevention of heat in female dogs. However, frequently an initial heat is observed shortly after the implant is inserted due to the flare-up effect (Fontaine and Fontbonne, 2011).

Androgens. Preparations of this group are widely used for female contraception. The use of injectable or oral testosterone derivatives prevents oestrus in females. The synthetic androgen mibolerone exists in the form of a commercial oral preparation (Cheque Drops) for dogs and cats in the United States (Eade et al., 2009). The formulation is characterized by anabolic and antigonadotropic activity of the hormone. If the treatment is implemented at least 30 days before the start of a pro-oestrus, the heat is suppressed. The treatment can be continued for two years. Longer administration is not recommended because of possible hepatotoxicity. After discontinuing, the subsequent oestrus occurs in a period of 1 to 7 months with an average of 70 days (Kutzler and Wood, 2006).

Immunocontraception. For a long time attempts are exerted to use immunological phenomena for contraception in animals. The main idea consists in the induction of antibodies directed against antigens playing an important role in reproduction. An antigen– antibody reaction should lead to infertility lasting as long as a sufficiently high level of specific

antibodies exists in the blood circulation. The main problem however is the choice of suitable antigen characterized by adequate immunogenicity in order to achieve a contraceptive vaccine (Munks, 2012).

Zona-pellucida antigens. The zona-pellucida is a non-cellular glycoprotein membrane covering the oocyte and (after fertilization) the embryo up to the late blastocyst stage, whereupon it brakes and disappears. Three major zonal glycoproteins with different molecular weight designated as ZP1, ZP2 and ZP3 have been isolated from the membrane. Apart from its structural function the zona-pellucida is of great functional importance. It contains sperm receptor sites, which allow fertilization. Antizonal antibodies do not allow fertilization, without affecting the hormonal activity. Experiments were conducted in dogs and cats by using both allogeneic or xenogeneic zonal antigens, in particular derived from swine oocytes, which are easy to obtain because of wide availability of fresh slaughter material. Also recombinant antigens, obtained by biotechnological methods were used (Eade et al., 2009).

Inorganic Chemostrilant

A) Zinc gluconate neutralized with arginine (zeuterin): This formulation of the chemical compound of zinc gluconate neutralized with arginine was developed to chemically sterilize male dogs. The formulation was initially developed by Pet Healthcare International; it received approval from the United States Food & Drug Administration (FDA) in 2003 and was distributed in the U.S. under the name Neutersol® until Early 2005. Zeuterin™ is a non-surgical sterilant for male dogs delivered via intratesticular injection. The ideal method of chemical sterilization needs to meet three key criteria to be regarded as a good alternative tosurgical sterilization. First, it has to be effective in a high percentage of treated animals. Second, it should have ahigh margin of safety, without adverse effects for the environment. Third, it has to be permanent and irreversiblefollowing a single treatment. The first product obviously fulfilling these criteria was zinc gluconate. It was firstdescribed by Fahim et al. (1993). Zinc gluconate was provided as a sterile aqueous solution containing 0.2 M zinc gluconate (13.1 mg/mL) neutralized to pH 7.0 with 0.2M I-arginine in glass vials containing 2 mL of readyto-use solution.c The drug was supplied with plastic calipers and instructions for measuring the width of each testicle; a dosing chart was used to correlate testicular width (10 to 27 mm) with volume of zinc gluconate (0.2 to 1.0 mL). In this project, dogs of all ages were treated by following the product label recommendation for volume of injection. Dogs with testes measuring < 10 mm in width received zinc gluconate volumes of 0.1 mL/testicle. Volumes for dogs with testes measuring > 27 mm in width were truncated at 1.0 to 1.1 mL/testicle (1.0 mL is the highest approved dose). The active ingredient is zinc gluconate neutralized with arginine. The formulation causes permanent sterility in one treatment, the process of neutering with Zeuterin is also known as "zinc neutering. the treatment with this chemical does not require general anesthesia, sedation is recommended to prevent movements of the dog during injection (Kutzler and Wood, 2006). Correct injection technique was foundcritical for the safe use of Neutersol in order to avoid ulceration of the scrotum and painful swelling of the testes (Kutzler and Wood, 2006).

The exact mechanism of action of Zeuterin is not known. The product is administered as an intratesticular injection into the center of the testicle via the dorsal cranial portion of testicle, parallel to the longitudinal axis. After injection, the compound diffuses in all directions from the center of the testis. In the concentration used, zinc gluconate acts as a spermicide and destroys spermatozoa in all stages of development and maturation (Massei and Miller, 2013). Zinc gluconate is absorbed and metabolized by the body within 72 hours after the injection. As the dog's body increases blood flow and creates inflammation to heal, it results inpermanent and irreversible fibrosis in the seminiferous tubules, rete testis, and epididymis. This process results in permanent sterilization, and the endocrine feedback system remains intact. Following injection, the testicles atrophy over a period of time ranging from weeks to months, resulting in a reduction in testicular size and changes in shape or texture. These changes may or may not be symmetrical.Hence, chemical castrationcould be an attractive option for developing countries with limited resources for surgical dog management programs (Garde et al., 2016).

B) Calclum chloride (cacl₂): Nonsurgical male sterilization techniques have been evaluated as a means to avoid the potential health complications, expense, expertise and facilities required for surgical sterilization procedures. One of the most promising is calcium chloride (CaCl₂), which has been utilized to chemically castrate a variety of species Calcium chloride (CaCl₂), delivered as intratesticular injection, is being researched as Inorganic Chemo-sterilants for dogs (Massei and Miller, 2013). Following intratesticular injection of CaCl₂, necrosis, fibrosis and degeneration of seminiferous tubules and Leydig cells occurs, reducing or eliminating the production of spermatozoa, testosterone and sperm counts in a dose-dependent manner in male dogs (Jana and Samanta, 2007). Calcium chloride dihydrate (CaCl₂) has been the subject of renewed interest as a potential injectable sterilizing agent for male dogs and cats that may reduce testosterone levels more significantly, and might carry less risk of severe injection-site reactions, than other injected sterilizing agents. Additionally, CaCl₂ has spurred discussion because it can be made from readily available ingredients, raising questions about the legality, ethics, appropriateness, and advisability of its use in the many countries in which Zeuterin/EsterilSoI is not available and is not projected to come to market in the immediate future. CaCl₂ was effective and economical for the sterilization of male dogs. It is free from pain and chronic stress and will contribute to a simple alternative (Jana and Samanta, 2007).

C) CaCl₂ formulation and dosing chart: The alcohol solution of 20% calcium chloride dihydrate is prepared by the veterinarian or by an accredited compounder. Prepare as follows: Formulation: 20 gr of pharmaceutical grade CaCl₂ (dihydrate) is brought to a final volume of 100 ml of 95% pharmaceutical grade ethanol, mixed, sterilized by autoclave or syringe filter and delivered in a stopper top container (Jana and Samanta, 2007). Always pull 0.2 ml of calcium chloride

over the maximum recommended dose. Up to 10% of dogs require up to 0.2 ml more calcium chloride in order to achieve a firm feeling upon injection. This includes large and small dogsas elongation of the testicle may change the required volume significantly (Oliveira et al., 2012). Supplies: Calcium chloride, Caliper, Luer lock syringes with 1" 23 gauge needles, Separate 1 $\frac{1}{2}$ " 23 gauge needles, Gauze in chlorhexidine solution mixedaccording to manufacturer's directions, Drugs for sedation,Ketophen or other pain management,Exam gloves if desired (Oliveira et al., 2012).

Chemo sterilization is hypothesized to result from edema that follows intratesticular injection of CaCl2, leading to necrosis and fibrosis and degeneration of seminiferous tubules (and germ cells) and the interstitial (Leydig) cells (Jana and Samanta, 2007). As testosterone concentrations fall, the integrity of the seminiferous tubule is further compromised. Have also proposed a role for free radicals in the mechanism of action of CaCl2 injection. According to this hypothesis, CaCl2 causes production of free radicals in testicular tissue, leading to lipid peroxidation and destruction of cellular structures, and also directly impairing spermatogenesis and androgenesis (Soumendra and Shyamal, 2017). Studies from this group have demonstrated decreased activities of catalase, glutathione peroxidase, glutathione S-transferase, and superoxide dismutase, decreased levels of reduced glutathione, and increased levels of conjugated dienes, with increased doses of CaCl2 (Jana, 2011).

Table 1 - Dosage and testicular width with their dose per testicle	
Testicular Width	Dose per testicle
10-14 mm and sexually mature adult cats	0.25 ml (if testis feels overly full, STOP before full dose)
15-18 mm	0.5 ml
19-22 mm	0.8 ml to 1 ml (continue to fullness)
23-24 mm	1 ml to 1.5 ml (continue to fullness)
25-26 mm	1.5 ml to 2 ml (continue to fullness)
27 mm and above	1.5 ml to 2.5 ml (continue to fullness)
Source: www.calciumchloridecastration.com/chemical-castration-instructions-for-veterinarians	

Hypertonic Sodium Chloride (NaCl)

Sodium Chloride Solution - hypertonic saline is a solution that is inexpensive and easy to administrate and revealed that severe degenerative changes in testicular seminiferous tubules and massive infiltration of immune cells in hypertonic saline group. Additionally researchers indicated that "intratesticular hypertonic saline injection seems to be an alternative method in the future to its rivals such as orchiectomy and medical castration" but that further laboratory work would be required to ascertain the potential utility of this approach in dogs (Emir et al., 2008). In other study, it was observed that 20% sodium chloride could be used for chemical castration in young dogs. It was suggested that intra testicular injection of hypertonic saline could be an effective method for nonsurgical sterilization of the non-adult male dogs but not adult dogs (Ibrahim et al., 2016). The hypertonic solution was prepared by dissolving NaCl (200 mg/mL) in ultrapure water. After dilution, the 20% NaCl solution was autoclaved in 50 mL glass flasks and stored at 5 C until use. The use of inorganic chemo-sterilants in male dogs is an attractive option because it removes the disadvantages and costs of surgical sterilization and post-operative care (Rojas et al., 2011). Furthermore, in regions where surgical castration of male dogs is not culturally accepted (e.g. Romania, the Bahamas) chemical castration offers a reasonable alternative (Garde et al., 2016). Hence, chemical castration could be an attractive option for developing countries with limited resources for surgical dog management programs (Garde et al., 2016).

Advantage and disadvantage of surgical Castration methods

A) Advantage of surgical castration methods: Surgical sterilization of dogs is one of the most commonly performed procedures in veterinary practice, and is done as a method of contraception to aid in the pet overpopulation problem, as well as to prevent diseases of reproductive system, such as benign prostatic hyperplasia and to modify undesirable behavior, such as internal aggression and mounting of other dogs, Will not be able to reproduce, will not get ovarian or uterine cancer, Will not have dangerous uterine infections, Will not mark territory by urinating or spraying, lessens tendency to fight with other animals despite castration is almost the sole method for control of pet's overpopulation globally.

B) Disadvantages and postoperative complications: For many years, surgical castration has been considered a standard gold tool for sterilization of male animals. However, several drawbacks have been associated with this procedure such as high cost, time consumption, need for postoperative care and management, risk of post-operative complications, small-scale application, the requirement of anesthesia, medical equipment, a sterile surgical suite, a trained veterinarian, recovery time, and incision site observation (Jana and Samanta, 2007). Surgical castration also do have complication such as, hemorrhage, wound dehiscence, infections, and scrotal swellings, requires anesthesia has some morbidity and mortality and expensive and technical also not available in much of world (Adin, 2011).

Advantages and disadvantage of non-surgical castration methods

A) Advantage of non-surgical castration methods: An ideal chemical sterilizing agent would be one that effectively arrests spermatogenesis and androgenesis as well as libido with absence of toxic or other side effects (Wiebe et al., 1989). Advantages of chemical castration are apparent reduction in pain and stress as well as elimination of hemorrhage, hernia, infection, myiasis and other surgical sequela. It is also suited for mass-scale sterilization, simple and inexpensive (Ibrahim et al., 2016). This method may offer savings in cost, time, and facility requirements, thus helping animal welfare organizations sterilize more animals and/or redirect resources to other lifesaving projects. It also presents an option for pet owners who would prefer to sterilize their dog without surgery. The low cost, ease of use, and cultural acceptance of a sterilization method that does not require removal of the testes make inorganic chemo-sterilants a valuable tool for large-scale sterilization campaigns, particularly in areas lacking clinical facilities or skilled staff (Levy et al., 2008).

B) Disadvantage of non-surgical castration methods: As a result of these chemical injections, side effects have been documented. The dog will experience pain in his scrotum for three to five days after the injections. There was swelling, redness, and irritation. Lethargy and diarrhea are known side effects that are usually temporary (Threlfall and Immegart, 2000).

CONCLUSIONS AND RECOMMENDATIONS

The use of fertility inhibitors is gaining acceptance to control populations of companion animals and wildlife. For dog population management, nonsurgical sterilization is increasingly advocated as deserving priority for development because of its potential to be more costeffective than surgical sterilization. For dog population management, nonsurgical or chemical sterilization is increasingly advocated as deserving priority for development because of its potential to be more cost effective than surgical sterilization. Chemical sterilization methods so far employed include hormonal methods, immunocontraceptives and Inorganic Chemo-sterilants such as calcium chloride-CaCl₂, zinc gluconate neutralized by arginine (Neutersol), sodium chloride-NaCl solution). This review indicated that the past decade saw a significant increase in studies concerning fertility inhibitors for dogs. If nonsurgical fertility control is chosen to manage dog populations or their impact, social acceptance, humaneness, effectiveness, feasibility, costs, and sustainability of this method should be evaluated at an early planning stage. This framework is based on the assumption that a set reduction of dog population size or the elimination of a disease such as rabies, within a predefined timeframe can be achieved by using nonsurgical fertility control as an additional tool to education and vaccination.

The trend of using calcium chloride should be adopted to the community; training should be given to the practitioners in the way how to inject the chemical into the testicle; the government should take into consideration in policy making in the application of calcium chloride for dog population control; further research should be conducted to reduce side effects of calcium chloride.

DECLARATIONS

Corresponding author

Dr. Addisu Mohammed Seid, Email: addisvet838@gmail.com

Acknowledgement

We would like to express our great acknowledgement to Dr. Tewodros Fantahun for his support through the whole process of developing this publication.

Authors' contribution

Dr. Addisu Mohammed Seid and Demr Abebe Terefe equally participated in the reviewing of this paper. We reviewed the paper and contributed in developing the content.

REFERENCES

- Abshenas J, Molaei MM, Derakhshnfar A, Ghalekhani N (2013). Chemical sterilization by intra-testicular injection of Eugenia caryophyllata essential oil in dog: A histopathological study. IJVS. 8(2): 9-15. (Google Scholar; Import into EndNote)
- Adin CA (2011). Complications of Overiohysterectomy and Orchiectomy in Companion Animal. Veterinary Clinics: Small Animal Practice. 41:1023 –1039. (Google Scholar; Import into EndNote)
- Briggs J (2012). Non-surgical methods of dog population control A brief overview of current and future opportunities. In Book of Abstracts of the 1st International Conference on Dog Population Management. FERA – Food and Environment Research Agency York, UK. (Google Scholar; Import into EndNote)
- Butler JRA, du Toit JT and Bingham J (2004). Free-ranging domestic dog (Canisfamiliaris) as predators and prey in rural Zimbabwe: threats of competition and disease to large wild carnivores. Biological Conservation 115: 369-378. (Google Scholar; Import into EndNote)
- Courchamp F, Grenfell B and Clutton-Brock T (1999). Population dynamics of obligate cooperators. Proceedings of the Royal Society of London B266, 557-563. (Google Scholar; Import into EndNote)
- Deressa A, Sefir D, Mamo H, Ali A, Akililu M, et al. (2013). Rabies diagnosis and surveillance for the period 2010-2012 in Ethiopia. 11th SEARG meeting, Dar es Salaam 11-15 February 2013, South Africa.
- Downes M, Canty MJ, More SJ (2009). Demography of the pet dog and cat population on the island of Ireland and human factors influencing pet ownership. *Preventive Veterinary Medicine*, 92: 140-149. (Google Scholar; Import into EndNote)

- Eade JA, Robertson ID, James CM (2009). Contraceptive potential of porcine and felinezonapellucida A, B and C subunits in domestic cats. Reproduction 137: 913–922. (Google Scholar; Import into EndNote)
- Emir L, Dadali M, Sunay M, Erol D, Caydere M and Ustun H. (2008). Chemical castration with intratesticular injection of 20% hypertonic saline: a minimally invasive method. In Urologic Oncology: Seminars and Original Investigations, 26(4), 392-396. (Google Scholar; Import into EndNote)
- Fahim MS, Wang M, Sutcu MF, Fahim Z and Yougquist RS (1993). Sterilization of dogs with intraepididymalinjection of zinc arginine. Contraception; 47: 107–22. (<u>Google Scholar</u>; Import into <u>EndNote</u>)
- FAO (2014). Dog Population Management FAO/WSPA/IZSAM Expert meeting. Banna, Italy, 14 -19 March 2011: Food and Agriculture Organization of the United Nations, Rome.
- Fontaine E and Fontbonne A (2011): Clinical use of GnRH agonists in canine and felinespecies. Reproduction in Domestic Animals 46(2): 344-53. (Google Scholar; Import into EndNote)
- Garde E, Pérez GE, Vanderstichel R, Dalla Villa PF, & Serpell JA (2016). Effects of surgical and chemical sterilization on the behavior of free-roaming male dogs in Puerto Natales, Chile. Preventive Veterinary Medicine, 123: 106-120. (Google Scholar; Import into EndNote)
- Garde, E, Acosta-Jamett G, Bronsvoort BM (2013): Review of the risks of some canine zoonoses from freeroaming dogs in the post-disaster setting of Latin America. Animals, 3: 855–865. (Google Scholar; Import into EndNote)
- Gobello C (2012). Effects of GnRH antagonists vs. agonists in domestic carnivores, a review. Reproduction in Domestic Animals. 47: 373– 376. (Google Scholar; Import into EndNote)
- Gupta SK and Bansal P (2010). Vaccines for immunological control of fertility. Reproductive Medicine and Biology, 9(2): 61–71. (Google Scholar; Import into EndNote)
- Haupt W (1999). Rabies-risk of exposure and current trends in prevention of human cases. Vaccine, 17(13): 1742-1749. (Google Scholar; Import into EndNote)
- Hughes J and Macdonald DW (2013). A review of the interactions between free-roaming domestic dogs and wildlife. *BiolConserv*; 157: 341–51. (Google Scholar; Import into EndNote)
- Ibrahim A, Ali MM, Abou-Khalil SN and Ali, FM (2016). Evaluation of chemical castration with calcium chloride versus surgical castration in donkeys: testosterone as an endpoint marker. BMC Veterinary Research, 12(1): 46. (<u>Google Scholar</u>; Import into <u>EndNote</u>)
- International Companion Animal Management Coalition (2007). Humane dog population management guidance. http://icamcoalition.org/Accessed, October 23: 2012.
- Jana K and Samanta PK (2007). Sterilization of male stray dogs with a single intratesticular injection of calcium chloride: a dosedependent study. Contraception, 75(5): 390-400. (<u>Google Scholar</u>; Import into <u>EndNote</u>)
- Jeong K-H, and Kaiser UB (2006). Chapter 31 Gonadotropin-Releasing Hormone Regulation of Gonadotropin Biosynthesis and Secretion. In Knobil and Neill's Physiology of Reproduction (Third Edition), J. Neill, T. Plant, D. Pfaff, J. Challis, D. de Kretser, J. Richards, and P. Wassarman, eds. (St Louis: Academic Press). 1635–1701. (Google Scholar; Import into EndNote)
- Khan MAH, Prevost M, Waterston MM, Harvey MJA, and Ferro VA (2007). Effect of immunisation against gonadotrophin releasing hormone isoforms (mammalian GnRH-I, chicken GnRH-II and lamprey GnRH-III) on murine spermatogenesis. *Vaccine* 25(11): 2051–2063. (Google Scholar; Import into EndNote)
- Kutzler M and Wood A (2006). Non-surgical methods of contraception and sterilization. *Theriogenology* 66(3): 514- 525. (Google Scholar; Import into EndNote)
- Levy JK, Crawford PC, Appel LD & Clifford EL (2008). Comparison of intratesticular injection of zinc gluconate versus surgical castration to sterilize male dogs. American Journal of Veterinary Research, 69(1): 140–143. (<u>Google Scholar</u>; Import into <u>EndNote</u>)
- Ludwig C, Desmoulins PO, Driancourt MA, Goericke-Pesch S, Hoffmann B (2009). Reversible down regulation of endocrine and germnative testicular function (hormonal castration) in the dog with the GnRH-agonist azagly-nafarelin as are movable implant "Gonazon"; a preclinical trial. *Theriogenology*, 71(7): 1037–1045. (Google Scholar; Import into EndNote)
- Macpherson CNL, Meslin FX, Wandeler AI (2013). Dogs, zoonoses and public health. Second edition. *Wallingford, UK: CABI International.* (Google Scholar; Import into EndNote)
- Massei G & Miller LA (2013). Nonsurgical fertility control for managing free-roaming dog populations: a review of products and criteria for field applications. *Theriogenology*, 80(8), 829-838. (Google Scholar; Import into EndNote)
- Matter HC & Daniels TJ (2000). Dog ecology and population biology. In: Macpherson, C., Meslin, F. & Wandeler, A. (Eds.) Dogs, zoonoses and public health. 50. Wallingford: CAB International Publishing. (Google Scholar; Import into EndNote)

Matznick-koler J (2002). The Origin of dogs revisited, Antrhrozoos, 15 (2): 98-118. (Google Scholar; Import into EndNote)

- Moges N (2015): Rabies in Ethiopia: Review Article. Academic Journal of Animal Diseases 4(2): 74–81, 2015. (Google Scholar; Import into EndNote)
- Munks MW (2012). Progress in development of immunocontraceptive vaccines for permanent non-surgical sterilization of cats and dogs. Reproduction in domestic animals, 47: 223–227. (<u>Google Scholar</u>; Import into <u>EndNote</u>)

Neutersol or package insert. Fayette, Mo: Addison Biological Laboratory Inc, 2003.

OIE (2009). Guidelines on stray dog population control. Terrestrial Animal Health Code. (Google Scholar; Import into EndNote)

- Pal SK (2005): Parenteral care in free-ranging dogs, Canisfamiliaris. Applied Animal Behaviour Science 90(1), 31-47. (Google Scholar; Import into EndNote)
- Reece JF, Chawla SK, Hiby EF, Hiby LR, (2008): Fecundity and longevity of roaming dogs in Jaipur, *India.* BMC Veterinary Research. 4(1): 6. (Google Scholar; Import into EndNote)

- Report of the Workshop, Entebbe, Uganda, 23–24 January (2013). Effective animal health-food safety surveillance capacity development in Eastern Africa.
- Rojas MAM, Rodríguez IMV & Tovar DS (2011). Métodos para el control de poblacionescaninas: unaintroducción. UnaSalud, 2(1), 63-79. (Google Scholar; Import into EndNote)
- Soumendra NK and Shyamal KD (2017). Chemosterilization induced by intratesticular injection of calcium chloride (cacl2) a tool for population control. International Journal of Pharmaceutical, Chemical & Biological Sciences, 7(1): 25-35. (Google Scholar; Import into EndNote)

TBoH (2012). Tigray National Regional State Bureau of Health Annual report, Tigray Mekelle, Ethiopia. (Link)

- Thompson DL (2000). Immunization against GnRH in male species (comparative as pects). Animal Reproduction Science, 60: 459–469. (Google Scholar; Import into EndNote)
- Threlfal WR and Immegart HM (2000). Evaluation of intratesticular injection of for chemical sterilization of dogs. American Journal of Veterinary Research, 61(5): 544–549. (Google Scholar; Import into EndNote)

WHO (1990). Guidelines for dog population management. WHO.ZOON 90.166, 6-37. (Google Scholar; Import into EndNote)

WHO (2005). World Health Organization expert consultation on rabies: first report. (Google Scholar; Import into EndNote)

- Wiebe JP, Barr KJ, Buckingham KD. (1989). Sustained azoospermia in squirrel monkey, saimirisciureus, resulting from a single intratesticular glycerol injection. Contraception, 39(4): 447–457. (Google Scholar; Import into EndNote)
- Wiebe VJ and Howard JP (2009). Pharmacological advances in canine and feline reproduction. Topics in Companion Animal Medicine, 24(2): 71–99. (Google Scholar; Import into EndNote)

www.calciumchloridecastration.com/chemical-castration-instructions-for-veterinarians

www.fao.org/docrep/018/i3391e/i3391e.pdf.

www.humanesociety.org/issues/pet_overpopulation/facts/pet_ownership_statistics.html