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Reproductive control in elephant: a tool for population and aggression management

Chaleamchat Somgird

Janine L. Brown

Chatchote Thitaram

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Chaleamchat Somgird[1,2] Janine L. Brown[3] Chatchote Thitaram[1,2*]

Abstract

Although Asian elephant is listed among the endangered species, the number of populations is over the carrying capacity in some areas, resulting in human-elephant conflict, as well as African elephants. High aggression associated with musth and female reproductive pathology are observed in captive elephants. Thus, population and aggression management through reproductive control is an alternative method for mitigating these problems. This article reviews methods of reproductive control in both Asian and African elephants with an overview of male and female reproductive physiology. Hormonal control and immunocontraception, i.e. porcine zona pellucida and gonadotropin releasing hormone (GnRH), are described for the control of reproduction, musth and reproductive pathology.

Keywords: elephant, reproductive and aggression control, immunocontraception, GnRH vaccine

[1]*Center of Excellence in Elephant Research and Education, Chiang Mai University, Chiang Mai 50200, Thailand*
[2]*Department of Companion Animals and Wildlife Clinics, Faculty of Veterinary Medicine, Chiang Mai University, Chiang Mai 50100, Thailand*
[3]*Smithsonian Conservation Biology Institute, Smithsonian Institution, Front Royal, VA 22630, USA*
***Correspondence**: chatchote.thitaram@cmu.ac.th*

Introduction

Asian elephant (*Elephas maximus*) is listed among the endangered species by the International Union for Conservation of Nature (IUCN). Its number in the wild continues to decline because of habitat destruction and poaching. African elephant (*Loxodonta africana*), whose number is 10 times greater than the Asian species, experiences similar problems. Even in some highly protected areas, the number of African elephant exceeds the carrying capacity, resulting in human-elephant conflict (HEC) (Perera, 2009). This is also a problem with Asian elephants in some countries, including Thailand. Thus, population management through reproductive control is an alternative method for mitigating these problems.

The control of reproductive function plays an important role in population management (see reviews: Kirkpatrick et al., 2011; Naz and Saver, 2016; Yitbarek and Regasa, 2014), also the control of behavior/musth aggressive behaviors in both wild and captive elephants (Bertschiger et al., 2004; De Nys et al., 2010; Stout et al., 2007), and reproductive pathology treatment (Boedeker et al., 2012). Permanent sterilization through the removal of ovaries or testes is difficult in elephant because of their large body size, anatomy (Foerner et al., 1994) (e.g. both male and female gonads are located inside the abdominal cavity), and accompanying risks of abdominal surgery with high abdominal pressure. Surgical castration has been accomplished in a few captive bulls while they were still young; however, this method is unacceptable for a bull that is needed for breeding. This article reviews methods of reproductive control in both Asian and African elephants with an overview of male and female reproductive physiology. These methods are important strategies to manage the populations of elephants under human care, and are being used with increasing success to control wild elephant population in nature to prevent overpopulation and accompanying problems of habitat destruction and HEC.

Reproductive physiology

Female: puberty and ovarian cycle: Puberty (i.e. initiation of ovarian cycles) in young female elephants occurs between the ages of 4 and 10 years (Brown, 2014; Hildebrandt et al., 2006; 2011) and depends on several factors such as birth origin (e.g. wild or captive), nutrition and resource availability, and growth rate. Cyclical changes in ovarian activity and structures are accompanied by changes in hormones of the hypothalamo-pituitary-gonadal (HPG) axis, including gonadotropin releasing hormone (GnRH) from hypothalamus, follicular stimulating hormone (FSH) and luteinizing hormone (LH) from anterior pituitary gland, estrogens during the follicular phase and progestagens (progesterone and related steroids) during the luteal phase from the ovary.

The normal estrous cycle of female Asian elephant is between 14 and 18 weeks in length with pregnancy lasting 20-22 months. The non-pregnant luteal phase, characterized by high circulating progestagen concentrations, ranges between 10-14 weeks, while the interluteal phase (or follicular phase) lasts between 3 and 6 weeks. During the follicular phases, two surges (peaks) of LH occur. The first LH surge is anovulatory (anLH), whereas ovulation occurs 3 weeks later around 24 hours after the second LH (ovLH) surge (Brown et al., 1999; Hermes et al., 2000; Kapustin et al., 1996). Thus, a female only has about three chances per year to conceive. Within each cycle, the fertile period is short, only from about 2 days before until shortly after ovulation.

Male: puberty and musth: The onset of male elephant puberty, based on initiation of testicular activity, varies between the ages of 6 and 10 years (Brown, 2014; Hildebrandt et al., 2006) and depends on the same factors as females. The seminiferous tubules commence spermatogenesis – a series of cell divisions and modifications necessary for the production of spermatozoa – as a result of changes in the pattern of secretion of the major reproductive hormones. This includes increased secretion of GnRH from the hypothalamus, FSH and LH from the anterior pituitary gland, and the secretion of androgens (mainly testosterone) from the interstitial cells of the testes.

Androgens are responsible for the development of secondary sexual characteristics and sex drive in male elephants. The secretion of testosterone is under the direct control of LH secretion from the pituitary gland and results in elevation of the blood. Testosterone production in elephants is related not only to age, but also to social hierarchy and dominance status. Elephant bulls exhibit a unique phenomenon, known as "musth", which is a circannual period of physiological, anatomical and behavioral changes in mature Asian and African elephant bulls (Ganswindt et al., 2005a; Ganswindt et al., 2005b; Rajaram, 2006; Sukumar, 2003). Typical musth signs are temporal gland secretions (TGS), continuous urine dribbling (UD), increased aggression, and elevated serum androgen concentrations (Ganswindt et al., 2005a; Ganswindt et al., 2005b; Rasmussen and Perrin, 1999; Rasmussen et al., 1984; Yon et al., 2008). Several factors are related to musth and its intensity such as age, nutrition, social status (hierarchy) and changes in HPG axis (Cooper et al., 1990; Lincoln and Ratnasooriya, 1996). A bull in musth shows behavioral changes, including increased aggression toward humans, dominant displays, and decreased response to commands. These changes are associated with serum testosterone concentrations that are 10 times higher or more than those of bulls during non-musth periods.

Reproductive control

Hormonal control: Ovarian and testicular functions are under hormonal control; thus, methods for altering HPG activity can be used to manipulate reproduction. Hormonal agonists and antagonists that disrupt the HPG axis have been used for reproductive control in elephants. Estrogen implantation was shown to prevent pregnancy in wild African elephant females (Delsink and Kirkpatrick, 2012; Stout and Colenbander, 2004). However, prolonged periods of estrus occurred, resulting in herd disruption, with treated females being harassed by bulls for breeding. Moreover, young calves were harmed because these harassed females stopped lactating, and they were also harmed by the bulls. Therefore, non-steroidal hormones such as GnRH agonists were applied to control the HPG axis in elephants. Leuprolide acetate (Lupron®; Tekada, Abbott), a GnRH agonist, reduced testosterone secretion during musth in elephant bulls, but repeated injections were needed (Brown et al., 1993; de Oliveira et al., 2004).

Immunocontraception: porcine zona pellucida vaccine: Today, the effective method of immunocontraception is used for inducing an active immune against native hormones or germ cells to prevent fertilization in elephants. One method which is very useful for reproductive control is vaccination against proteins in the egg zona pellucida (ZP) (Delsink and Kirkpatrick, 2012). The anti-pig ZP vaccine (pZP) is produced using ova obtained as a by-product of the pig slaughter industry. In general, ZP is a non-cellular capsule that surrounds all mammalian eggs. Its structure consists of glycoproteins. The backbone glycoprotein (ZP1) has been well conserved in evolution and shows great similarity among species (fish, amphibians, avian and mammal). Other glycoproteins (ZP3 and ZP2) are primary components of the sperm receptor, which permits sperm and egg binding during fertilization. In elephant females, the ovum binds to antibody on all surfaces of ZP. Consequently, sperm binding sites are blocked and sperm cannot penetrate to fertilize the ovum, resulting in no pregnancy (Perdo et al., 2007).

In one field study in Africa, several females were vaccinated with an initial dose of 400 µg (intramuscular injection) followed by two 200 µg boosters at 5- to 7-week intervals, and then with subsequent 200 µg annual boosters (Delsink and Kirkpatrick, 2012). This vaccination program decreased the population growth rate from 10 to 0% in just a few years (Bertschinger, 2010, Delsink and Kirkpatrick, 2012). PZP vaccine has many advantages: it has high contraceptive efficacy (at least 90%) with no negative effects on social behavior; it is safe and does not affect health or pregnancy; it is cost-effective and reversible; and the contraceptive agent does not pass through the food chain (Delsink and Kirkpatrick, 2012; Perdo et al., 2007). However, pZP vaccination is only useful in females for blocking the sperm receptor on eggs. Therefore, to affect specifically the HPG and control sex hormone production in both elephant sexes, other immunocontraceptive methods have been utilized.

Immunocontraception: hormone-based vaccine: The best hormone-based vaccines are against gonadotropin-releasing hormone (GnRH) and have been developed to suppress sex hormones (immune-castration) and aggressive or sexual behaviors in many animals such as pigs and horses. GnRH vaccines produce anti-GnRH antibodies in numerous domestic animal and wild species for contraceptive and aggressive sex-related behavior control (Kirkpatrick et al., 2011; Turkstra, 2005). GnRH is a deca-peptide hormone that regulates the reproductive HPG axis. GnRH vaccine is made using a synthetic GnRH tandem peptide conjugated with protein, such as ovalbumin. Anti-GnRH antibodies block native binding of GnRH to gonadotropin receptors in the pituitary gland (Stout and Colenbander, 2004). HPG axis function is inhibited, and reduces the release of LH and FSH from the pituitary, subsequently decreasing gonadal steroid hormone secretion and associated reproductive activities. The vaccine is effective in both sexes, is easy and safe to use, including in pregnant females, and is low in cost (Turkstra, 2005). Another advantage is that it appears to be reversible with short-term use, with reproductive activity returning to normal within few months after the last vaccination (Bertschiger et al., 2004; Kirkpatrick et al., 2011).

Male: musth and aggression control: GnRH vaccine has been used to control reproductive and sex-related behaviors that are testosterone driven (Bertschiger et al., 2004; De Nys et al., 2010; Lueders et al., 2014; Somgird et al., 2016a). The aggressive and/or musth behavior control or management in elephant bull is very important, especially in captivity. In one study of a captive African elephant bull, serum LH surge-like increases occurred about 4 weeks before the musth period, then was maintained at high levels for 5 weeks (Kaewmanee et al., 2011). In Asian elephant bulls, LH responses to GnRH challenge were greatest in the pre-musth period (about 1-2 months before musth onset), which is when serum LH and testosterone are increasing (Somgird et al., 2016b). Therefore, GnRH vaccine should be given prior to the predicted musth period to block the HPG axis and decrease aggressive behaviors that are driven by testosterone, perhaps making them easier and safer to handle in captivity.

Free range and captive African and Asian elephant bulls have been immunized with GnRH vaccines to suppress aggressive musth behavior. Asian elephant bulls were administered with 600 µg GnRH peptide approximately 2 months prior to expected musth, resulting in a postponement of musth for 2-6 months, shortening the musth duration (Rajapaksa et al., 2010; Somgird et al., 2016a), and completely stopping musth in a young Asian bull (Lueders et al., 2014). Serum LH and testosterone were decreased when anti-GnRH antibodies were elevated, and no UD was observed in a musth bull after completion of the vaccination program (Somgird et al., 2016a). Similarly, African elephant bulls exhibited lower fecal androgen metabolite concentrations after GnRH vaccination, and musth behavior was suppressed (Bertschiger et al., 2004; De Nys et al., 2010; Stout et al., 2007). However, some vaccinated Asian elephant bulls retained aggressive behaviors because of dominance in the facility. Therefore, GnRH vaccine might not suppress all aggression related to a hierarchy status, or individual learned experiences (Somgird et al., 2016a). A suppressive effect of GnRH vaccine on reproductive organs was reported in a young Asian bull treated over several years, including reduced sperm production and size of reproductive organs, i.e. ampulla, seminal vesicle, testicular with amorphous shape, and penis (Lueders et al., 2014).

One trial was performed on an aggressive human-killing bull at the elephant facility in Lampang province. The bull was monthly administered with GnRH vaccine (Improvac®) at the dose of 1,200 µg for 8 consecutive months. The aggression score, developed by Somgird et al. (2016a), was gradually reduced from five to two within the treatment period (unpublished data), with a capability of human approach. Thus, a high and continuous dose of GnRH vaccine could be used to control high aggression in elephant. However, the aggression in female elephants was observed, but not investigated and studied yet. This vaccine might have potential for controlling aggression as well.

Female: estrous cycle and reproductive hormone control: Gonadal hormones were controlled in female Asian elephants using GnRH vaccines. Serum progesterone was decreased after the last vaccine booster and remained low for several months, resulting in no cycling (Rachapaksa, personal communication). However, a similar GnRH vaccine failed to induce anestrus in African elephants (Valades et al., 2012). A rise in anti-GnRH antibody titers in elephant occurred and remained elevated for a few months after the last booster, same as in other species (Somgird et al., 2016a). An increasing dose of GnRH vaccine induced high titers and successfully down regulated the HPG axis in a female Asian elephant treated for reproductive tract pathologies (Boedeker et al., 2012), i.e. leiomyoma, a female reproductive pathology. GnRF vaccination was performed in female white and Indian Rhinoceros to reduce the size of uterine leimyomas (Hermes et al., 2016). This uterine tumor was suspected to be caused by continuous cycling without conception, with a negative impact on reproductive health (Hildebrandt et al., 2006). Thus, temporarily shutting down the ovarian cycle might help to reverse this pathology.

Previous studies indicated that several boosters were necessary to increase the efficiency of the vaccine and titers (Bertschiger et al., 2004; De Nys et al., 2010; Lueders et al., 2014; Rajapaksa et al., 2010; Somgird et al., 2016a; Stout et al., 2007), as well as other hormone-based vaccines (e.g. inhibin vaccine) (Medan et al., 2004). A common vaccine protocol is to start with a 600 μg initial dose and two boosters or more at 4-week intervals, followed by boosters every 6 months (Lueders et al., 2014; Rajapaksa et al., 2010).

Conclusion

Several methods have been used for the control of population growth and aggression in elephants, and have been shown to have advantages and disadvantages. These should be critically considered and used with care, particularly on wild elephants because of the need for repeated boosters of individual animals. There are advantages of GnRH vaccines over pZP immunocontraception when the purpose is for elephant management of both sexes, and in wild and captive settings. Further studies are needed to determine the ideal or suitable doses, booster intervals and vaccine formulas for each contraception, and any effects on short- and long-term reproductive potential and health.

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บทคัดย่อ

การควบคุมระบบสืบพันธุ์ในช้าง: เครื่องมือในการจัดการประชากรและความก้าวร้าว

เฉลิมชาติ สมเกิด[1,2] เจนีน แอล บราวน์[3] ฉัตรโชติ ทิตาราม[1,2]*

ช้างเอเชียจัดเป็นสัตว์ที่อยู่ในภาวะสัตว์ใกล้สูญพันธุ์ แต่จำนวนประชากรกลับมีปริมาณที่มากเกินความสามารถที่จะรับได้ ในบางพื้นที่ป่า ซึ่งส่งผลให้เกิดปัญหาความขัดแย้งระหว่างคนและช้าง ซึ่งปัญหานี้เกิดเช่นเดียวกันในช้างอาฟริกา นอกจากนี้ การตกมัน ความก้าวร้าวและพยาธิสภาพทางระบบสืบพันธุ์ในช้างเพศเมีย เป็นสิ่งที่เกิดขึ้นและตรวจพบได้ในช้างเลี้ยง ดังนั้นการควบคุมระบบสืบพันธุ์จึงเป็นทางเลือกหนึ่งที่ใช้ในการจัดการประชากรช้างและความก้าวร้าวในช้าง บทความนี้ได้ทบทวนวิธีการในการควบคุมระบบสืบพันธุ์ในช้างเอเชียและอาฟริกา รวมทั้งอธิบายสรีรวิทยาทางระบบสืบพันธุ์ของช้างเพศผู้และเพศเมีย การควบคุมระบบสืบพันธุ์ด้วยฮอร์โมน และการคุมกำเนิดด้วยภูมิคุ้มกัน เช่น วัคซีนพอร์ไซน์โซน่าเพลลูซิดา และวัคซีนโกนาโดโทรปินรีลิสซิ่งฮอร์โมน เพื่อใช้ในการควบคุมระบบสืบพันธุ์ การตกมัน และพยาธิสภาพทางระบบสืบพันธุ์ในช้าง

คำสำคัญ: ช้าง การควบคุมระบบสืบพันธุ์และความก้าวร้าว การคุมกำเนิดด้วยภูมิคุ้มกัน วัคซีนโกนาโดโทรปินรีลิสซิ่งฮอร์โมน

[1]ศูนย์ความเป็นเลิศด้านการศึกษาและวิจัยช้าง มหาวิทยาลัยเชียงใหม่ อ.เมือง จ.เชียงใหม่ 50200

[2]ภาควิชาคลินิกสัตว์เลี้ยงและสัตว์ป่า คณะสัตวแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ ต.แม่เหียะ อ.เมือง จ.เชียงใหม่ 50100

[3]สถาบันชีววิทยาการอนุรักษ์สมิธโซเนียน สถาบันสมิธโซเนียน ฟรอนท์รอยัล วีเอ 22630 สหรัฐอเมริกา

***ผู้รับผิดชอบบทความ** E-mail: chatchote.thitaram@cmu.ac.th*