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Parenteral administration of medroxyprogesterone acetate in cats: A morphological and histopathological evaluation of ovaries

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ABSTRACT

Fertility control measures aim to reduce reproduction and address the issue of overpopulation in pets. Progestins are among the most often utilized drugs for feline contraception, with Medroxyprogesterone acetate (MPA) being one of the most frequently employed progestins. This study aims to observe the effects of a single intramuscular injection of MPA at a dosage of 50 mg per cat on the ovaries of female cats. Twenty adult indigenous female cats were selected to evaluate the effectiveness of MPA for 42 days. The cats were divided into control and treatment groups. Cats in the treatment group received a single 50 mg intramuscular injection of MPA. Both groups had an ovariohysterectomy after 42 days. Behavioral changes in cats following ovariohysterectomy, along with a morphological and histopathological examination of the ovaries, were observed. Mean and standard deviation of ovarian length and width were measured in both the control and treatment groups. Study results showed a significant ($p < 0.05$) reduction in ovarian size in the treatment group compared to the control group. The average ovarian length and width were 0.85 ± 0.10 vs 0.72 ± 0.11 cm and 0.60 ± 0.07 vs. 0.51 ± 0.08 cm in the control and treatment groups, respectively. Three out of ten female cats in the treatment group developed follicular cysts, while none in the control group experienced them. Histological slides revealed ovarian atrophy and cessation of folliculogenesis. Therefore, these results suggest that a single 50 mg dose of MPA could be advantageous for controlling cat fertility and tackling the problem of overpopulated pets.

INTRODUCTION

Cats have coexisted with humans for a long time, but they are different from other tamed animals because they have a lot of freedom in how they behave and reproduce [1]. Cats are highly popular and widely kept as pets worldwide. Approximately 480 million cats are stray, whereas over 350 million cats live in households with their human friends. Cats are long-day breeders and can experience many estrus cycles during a breeding season, unless they become pregnant or sick [2]. The size of a cat litter varies between 3.7 and 4.6 kittens [3]. The breeding lifespan of a cat is around 10 years, and a female cat (queen) can produce up to 100 kittens throughout her lifespan [4]. If two cats in their reproductive stage were to hypothetically produce three litters of four kittens each year, the population would grow exponentially, reaching a staggering 20,736 cats in just four years [5]. Throughout the breeding season, female cats typically exhibit estrus activity at intervals of approximately two to three weeks, unless specific

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circumstances arise, such as pregnancy, pseudopregnancy (ovulation without fertilization), sterilization, or a serious illness [4]. The substantial fecundity of cats, coupled with extensive populations of free-roaming cats in several countries, has made the regulation of feline reproduction a subject of contention in many nations worldwide during the past few decades [6].

The global increase in the feline population leads to significant distress and necessitates the practice of euthanasia [2]. The main objective of controlling fertility in both feral and domesticated cats is to limit reproduction and avert pet overpopulation. This is an essential action for safeguarding the welfare of felines [5]. Surgical sterilization has been the sole reliable and long-lasting method of contraception for a considerable time [7]. If a lifelong state of infertility is desired, the most obvious operation to consider is ovariohysterectomy, which is expensive, invasive, and permanent. While surgical contraception is really very successful, it may not always be the preferred approach by pet owners. This is mostly due to the fact that it is irreversible, with the latter being particularly significant for cat breeders [5,8]. Therefore, many owners, particularly cat breeders, occasionally prefer temporary suppression of estrus by using different kinds of drugs such as medroxyprogesterone acetate (MPA), proligestone, megestrol acetate, chlormadinone acetate, levonorgestrel, altrenogest, etc. [6,9]. Contraceptives are utilized in cats for several objectives, including the maintenance of reproductive fertility in breeding specimens, the inhibition of sexual function in animals scheduled for surgery, and the mitigation of feral cat populations [10]. Pharmaceutical chemicals called progestins or progestogens (PG), which are synthetic versions of progesterone, are commonly used to control the reproductive cycle of domestic animals [11]. MPA is a progestin that is used to prevent female dogs and cats from entering the estrus cycle [12]. Progestins have demonstrated efficacy and cost-effectiveness as contraceptives for felids. However, it is important to consider the significant adverse effects associated with their use [13].

The least effective dosage of MPA is 2 mg/kg every 3 to 4 months or 3 to 5 mg/kg every 5 to 6 months [14,15]. However, the dose of MPA at 75 to 100 mg/cat is also used for feline contraception [16,17]. The elevated dosage of MPA correlates with an enhanced risk of adverse effects, including cystic ovaries, uterine pathologies like endometritis, cystic endometrial hyperplasia, pyometra, and uterine neoplasms, a heightened occurrence of mammary gland disorders (mammary gland hyperplasia, mammary neoplasms, and increased prolactin secretion), adrenocortical suppression, acromegaly, polydipsia, polyphagia, and diabetes mellitus [15,18,19]. Therefore, it is essential to determine a lower and effective total dose of MPA that can control fertility while minimizing potential side effects. Muphung *et. al.,* 2009, reported that a 50 mg/cat dosage of MPA can cause endometrial proliferation, but its effect on the ovaries was not documented [20]. Based on these findings, this study aims to use a single dose of MPA at a dosage of 50 mg/cat to observe whether this dosage is effective for suppressing estrus in cats for at least two estrus cycles or 42 days. Most studies suggest that repeated and long-term use of MPA can cause mammary gland changes in cats [18,21,22]. As this study is aimed at the observation of the effects of MPA after a single dose, mammary gland changes were not regarded. Although previous studies have explored the use of MPA at higher doses, limited data exist on the histopathological outcomes following a single 50 mg dose in cats. Therefore, this study aims to examine the morphological and histopathological effects of a single intramuscular injection of MPA at a dosage of 50 mg per cat on the ovaries.

MATERIALS AND METHODS

Experimental animals

The ethical approval for this study was issued as the ethical code for grant number FVMAS/AREC/2023/2 from the Animal Research Ethics Committee of Gazipur Agricultural University (GAU), Gazipur, Bangladesh.

For this experiment, a total of 23 animals were utilized, consisting of 20 adult female cats and 3 adult male cats, all aged between 12 and 18 months. The male cats were employed to examine the behavioural alterations in the female cats resulting from their presence. The body weight of the female cats varied between 2.5 and 4.0 kg. The cats were bred at least once before this experiment. The animals were acquired from several homes in the Gazipur area with their explicit permission. All the animals exhibited good health and showed no apparent signs of any health issues. The animals were raised in a specialized housing system, including both cage and free-roaming facilities at the Department of Surgery and Radiology at GAU. Each cat was accommodated in a stainless-steel cage (about 3' × 2') that ensured sufficient ventilation and view to adjacent cats. The entire area was surrounded by wire mesh and shade netting to preserve ecological complexity and control temperature. The facility had daily cleaning, and the litter trays were cleaned regularly. Behavior was evaluated both in person and via CCTV camera (Xiaomi Mi MJSXJ05CM 360° Motion Detection WiFi Security Camera®, Xiaomi, China) to identify signs of health, activity, and estrus. A 12:12 light-dark cycle was sustained by employing a curtain that enveloped the whole shed. During untreated periods, the cats were restricted to little activity inside a confined space, including a sandy substrate. The cats were provided with food and water ad libitum. The diet consists of boiled chicken, boiled fish, and boiled vegetables, including pumpkin, potato, and carrot. Prior to the commencement of the trial, the animals underwent a 14-day quarantine period in a separate housing system. The cats were immunized against rabies (Rabies Killed Vac®, Komipharm International Co., Ltd., Korea) after a period of 14 days using a single 1 ml subcutaneous injection. The cats were immunized against feline calicivirus, feline panleukopenia, feline rhinotracheitis, and *Chlamydia Psittaci* using the PUREVAX® Feline 4 vaccine (Boehringer Ingelheim Animal Health USA Inc., USA) as a single 1ml subcutaneous injection. After a period of 15 days following immunization, the cats underwent deworming treatment using Tab. Helminticide-L® (General Drugs House Co. Ltd., Thailand) at a dosage of 1 tablet per 10 kilograms of body weight, given orally on day 0 and day 6.

Experimental design

About 20 female cats that appear to be in good health were utilized in this study with the authority's permission and in accordance with its rules and suggestions. These cats were divided into two groups as follows: a) Control group had 10 female cats in which no MPA were administered, and ovariohysterectomy was performed after 42 days, and b) Treatment group had 10 female cats in which MPA (50 mg/cat) were administered and ovariohysterectomy was performed after 42 days.

In the treatment group, the animals were injected with MPA when they were not in estrus and certainly not showing any signs of estrus.

After adopting the cats with proper history, they were checked thoroughly for any health problems. Before the experiment, a veterinary ultrasound device (4Vet Slim ultrasound scanner®, Draminski Technology, Poland) was used to perform ultrasonography in order to rule out the potential of any ovarian cysts in these cats.

There were no visible cysts in the ultrasound images. The animals of the control group were not given any drugs, including antibiotics, anti-inflammatories, antihistamines, or hormones, prior to surgery, therefore serving as the control group. The treatment group received a single intramuscular injection of 50 mg MPA (Soma-JECT®, Social Marketing Company, Bangladesh). The absence of vaginal cytology facilities limited the precise determination of MPA administration timing at specific stages of the estrous cycle. However, it was ensured that, during the MPA administration, the cats exhibited no indications of estrus. A total of 10 female cats from the control group were examined for any abnormalities, and ovariohysterectomy was conducted on day 42. Samples were taken from the ovaries of all 20 female cats of both groups on the enumerated dates. Throughout this duration, vigilant observation was conducted on all the cats to detect any changes in their behaviour, such as rolling on the ground, excess vocalization, copulation, etc. The cats received standardized care following the procedure, including the administration of postoperative drugs. The post operative medicines include antibiotic, ceftriaxone at 50 mg/kg body weight IM once daily for 5 days (Inj. Topcef vet®, Navana Pharmaceuticals Ltd., Bangladesh), anti-inflammatory, tolfenamic acid at 4 mg/kg body weight IM once daily for 3 days (Inj. Tufnil vet®, Eskayef Pharmaceuticals Ltd., Bangladesh), antihistaminic, chlorpheniramine maleate at 2 mg/cat IM once daily for 3 days (Inj. Renacin vet®, Renata Ltd., Bangladesh), topical antiseptic, povidone iodine for dressing (Sol. Povin vet®, Opsonin Pharma Ltd., Bangladesh) and local antibiotic, Neomycin Sulfate and Bacitracin Zinc (Pow. Nebanol®, Square Pharmaceuticals PLC, Bangladesh). The data and sample were collected and analyzed. The ovaries were prepared for histological examination, and histopathological photographs were captured for analysis.

Ovariohysterectomy and sample collection

Following 12 hours of withholding feed from the female cats, they were anesthetized using a combination of ketamine HCl (Ketalar®, Popular Pharmaceuticals Ltd., Bangladesh) at 17 mg/kg body weight and Xylazine HCl (Xyla®, Interchemie, Netherlands) at 0.5 mg/kg body weight intramuscularly (IM) before performing ovariohysterectomy. As a premedication, atropine sulphate (Inj. Tropin vet®, ACME Laboratories Ltd., Bangladesh) at 0.065 mg per kg body weight IM was used. For maintenance, half of the initial dose of ketamine HCl was used. After induction, the surgical site was clipped, shaved, and disinfected. The site of incision was a ventral midline incision on the linea alba caudal to the umbilicus. After locating the uterine horns, the uterus, along with the ovaries, were incised and removed after ligating the major blood vessels using catgut 2-0 (Trugut®, Healthium Medtech Limited, India), and vicryl 2-0 (Trusynth®, Healthium Medtech Limited, India). After the surgery the animals were transferred to their shelter, and post-operative medications were administered as mentioned earlier. The ovaries were separated from the surrounding attachments for further assessment.

Morphological evaluation of ovaries

After collecting the ovaries, the shape and size were observed and photographed. The ovaries were assessed with a standardized scale, and the dimensions were measured.

Histopathological study

The study was done using the standard hematoxylin (BioGnost Hematoxylin H®, BioGnost Ltd., Croatia) and eosin (BioGnost Eosin Y 1% aqueous®, BioGnost Ltd., Croatia) staining procedure with slight adjustments. Initially, the tissues were preserved by immersing them in a solution of 10% formalin for a duration of 1 week. Subsequently, the tissues were thoroughly washed in flowing water overnight to eliminate the fixative. To dehydrate the tissues, they were sequentially immersed in increasing concentrations of alcohol, starting with 70%, 80%, 95%, and finally 100% for 2 hours each. The alcohol solution was changed every 2 hours. Then the tissues were kept in xylene for 2 hours before impregnation. At a temperature of 60 °C, the tissues were immersed in molten paraffin wax. This process involved two changes, with each change lasting one hour. Paraffin blocks were created by using rings and placing tissue pieces in the middle. The paraffin blocks that had been made were left at room temperature for a few hours. Subsequently, the tissues were sliced into sections of 5 µm thickness using a rotary microtome (Leica RM2125 RTS®, Leica Biosystems, Germany). The sections were immersed in the heated water (45 °C) within the hot water bath (Leica Water Bath HI1210®, Leica Biosystems, Germany). Next, the required tissue sections were placed on glass slides that were free from grease and oil. The prepared slides were air-dried and stored in a fridge at 4 °C until further use. The histopathological slides were analyzed, and the images were retrieved using the photomicroscope (Leica DM2500 & DM2500 LED Optical microscope®, Leica Biosystems, Germany).

Statistical analysis

The data were analyzed using SPSS Statistics®, Version 26.0 (IBM Corp., USA) to calculate the mean, mode, median, and standard deviation. Due to the data's deviation from normal distribution (shown by the Shapiro-Wilk test, $p < 0.05$), a Mann-Whitney U test was employed to compare the length and width of the ovaries of the control and treatment groups. The p-value of less than 0.05 ($p < 0.05$) was considered to be significant.

RESULTS

Effect of MPA on behavioral changes in the cat

The cats of the control group showed the signs of estrus, which include rolling on the ground, being loudly vocalized, vaginal swelling, etc. The average time of showing signs of estrus was 5.6 days, but they were not allowed to mate with the male cats. Among the 10 cats of the treatment group, 2 cats showed signs of estrus, such as vocalization and rolling on the ground, and the average time of estrus was 2.5 days (Table 1). They were housed in the same enclosure as the male cats. However, no mating behavior was observed in any of the treated female cats.

The estrus signs exhibited by the female cats in both groups were comparable. However, the cats in the treatment group displayed these signs for a shorter duration and showed no mating behaviour or interest in males.

Table 1. Behavioral changes of cats between the control and treatment groups.

Groups	Sample size (n)	No. of cats showing signs of estrus	Average time of estrus (days)
Control	10	10	5.6
Treatment	10	2	2.5
Total	20		

Alterations in ovarian morphology following MPA administration

The morphological findings of this study indicate a change in size (length and width) and shape of the ovaries after administration of MPA. The average length of the ovary in the control groups was 0.85 ± 0.10 cm, which is within the normal range. The shape was oval with follicles and corpus luteum present on the ovarian surface. The treatment group had an average ovary length of 0.72 ± 0.11 cm (without cysts) (Table 2). The length of the ovaries was significantly reduced in the treatment group (p = 0.0008). Data were presented as mean ± SD. Statistical significance was tested using the Mann-Whitney U test, where $p < 0.05$ was considered to be significant. The Mann-Whitney U test revealed significant differences between the control and treatment groups for both length (U = 320.5, p = 0.0008) and width (U = 303.0, p = 0.0035), indicating a substantial effect of the treatment on ovarian metrics.

The ovarian size in the treatment group was significantly smaller than the control group (Figure 1).

Table 2. Changes in the length and width of the ovaries.

Groups	Length (cm)	Width (cm)	Mann-Whitney U	p value
Control (Mean ± SD)	0.85 ± 0.10	0.60 ± 0.07	320.5	0.0008
Treatment (Mean ± SD)	0.72 ± 0.11	0.51 ± 0.08	303.0	0.0035

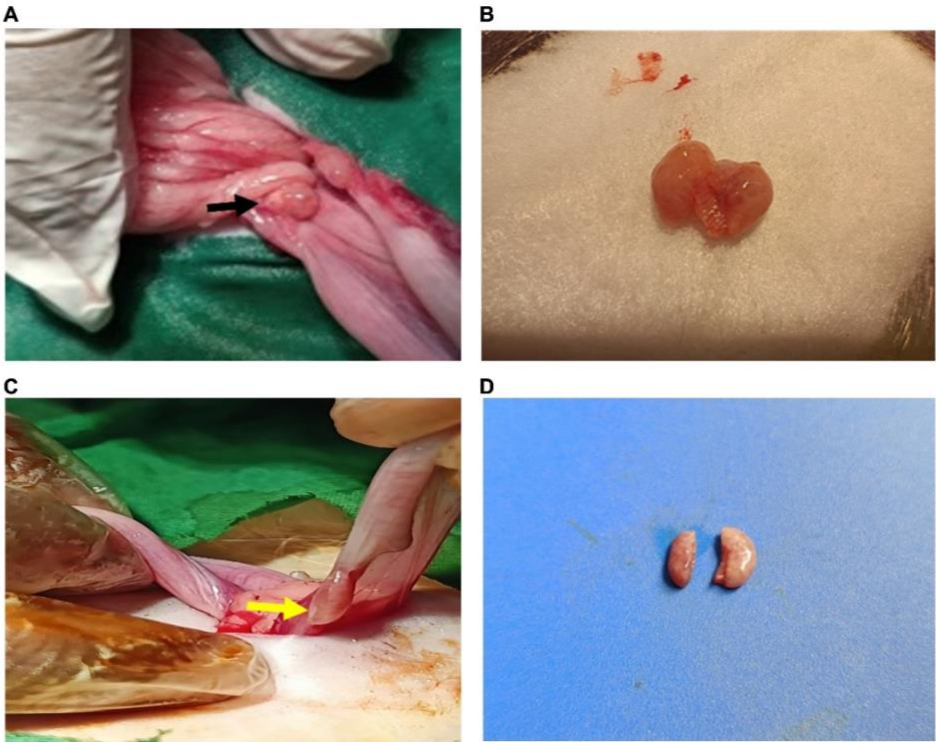

Figure 1. A comprehensive morphological observation of cat ovaries in the control (n = 10) and treatment group (n = 10). A) and B) exhibit normal, oval-shaped ovaries (black arrow) from the control group. These ovaries possess the appropriate size and morphology. C) and D) show ovaries from the treatment group (yellow arrow), which are smaller and flattened in shape.

The width of the ovaries of the control group was 0.60 ± 0.07 cm, whereas in the treatment group, it was 0.51 ± 0.08 cm (p = 0.0035). The follicles were absent on the surface (Table 2). In the treatment group, the ovaries were thinner and reduced in size. The shape was changed from oval to flat oval-shaped.

None of the cats in the control group revealed ovarian cysts. However, among the ten cats in the treatment group, three developed ovarian cysts. All of the cysts were unilateral follicular cysts (Figure 2).

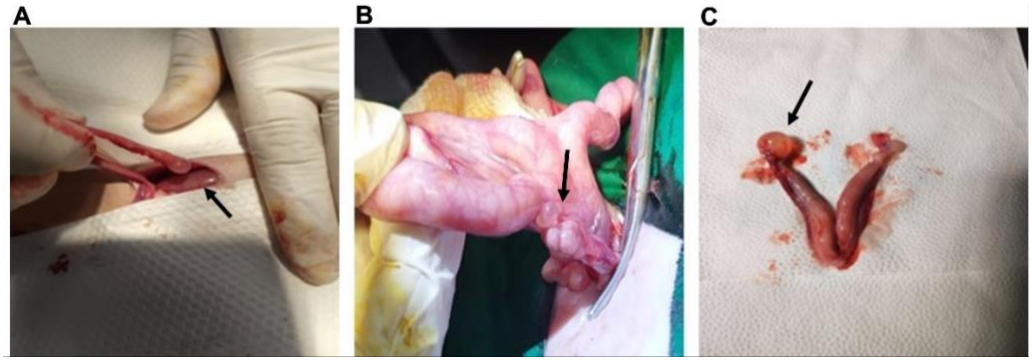

Figure 2. Gross presentation of ovarian follicular cysts in the treatment group, observed 42 days after MPA administration. A) and B) show the fluid-filled oval-shaped cysts (black arrows) during surgery, and C) indicates the removal of the cyst after ovariohysterectomy.

Histopathological alterations of MPA on the ovarian follicles

The ovaries collected from the female cats of the control group displayed follicles at various developmental stages. The primary, secondary, tertiary, and Graafian follicles were present in these ovaries. The presence of the corpus luteum was also visible in the histology slides (Figure 3). In the treatment group, the ovaries were shrunken, and there were no visible tertiary or Graafian follicles. Most of the follicles were primordial follicles (Figure 4).

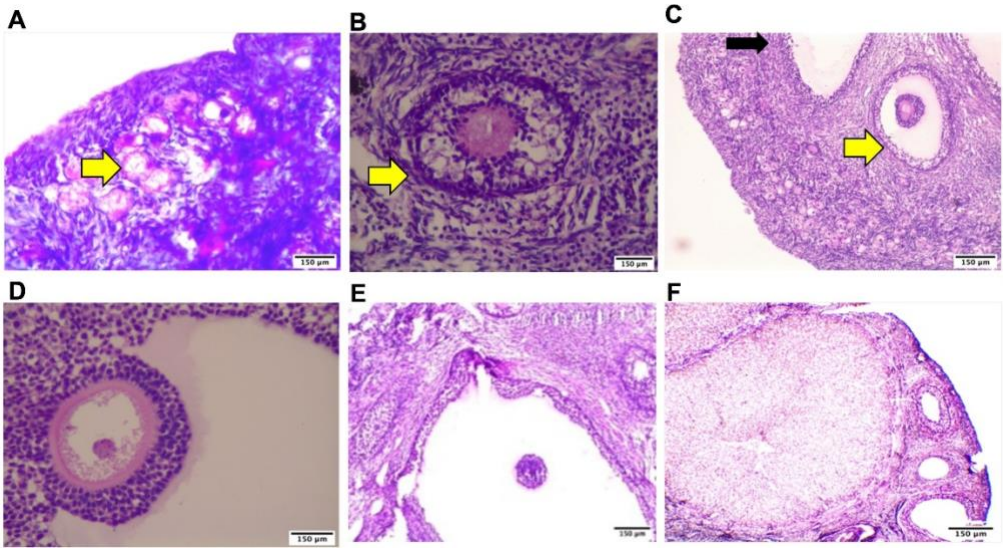

Figure 3. Histopathological sections of cat ovaries from the control group (n = 10), stained with hematoxylin and eosin (H&E) stain. This figure displays typical folliculogenesis and luteal features, including: A) primordial follicles, B) primary follicle, C) secondary follicle, D) ovum within a follicle, E) Graafian follicle, and F) corpus luteum.

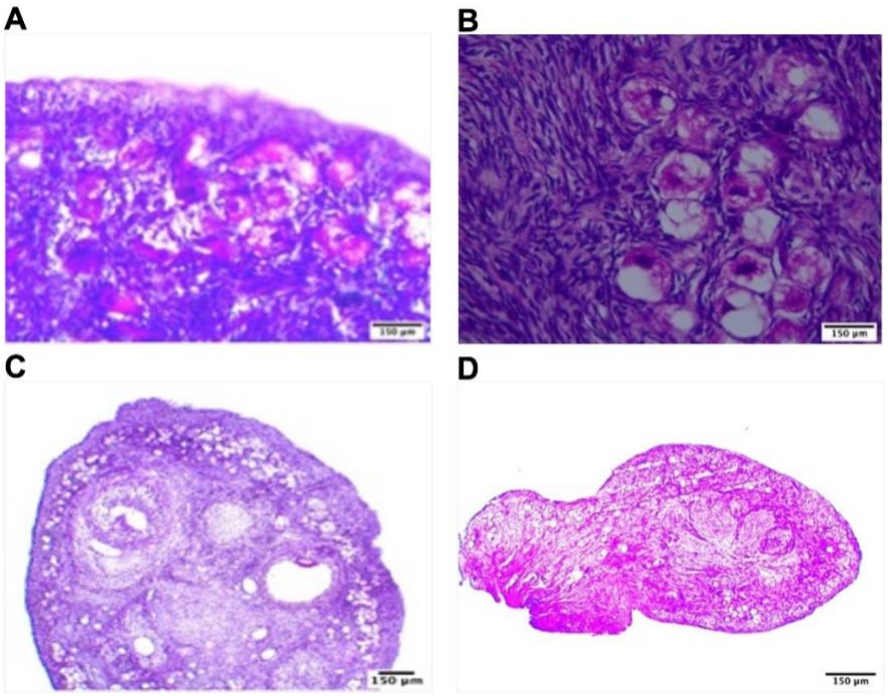

Figure 4. Histopathological sections of cat ovaries from both groups, following 42 days, showing primordial follicles and ovarian size. A) indicates the primordial follicles from the control group, and B) indicates the primordial follicles from the treatment group. C) shows the normal size of a cat's ovary in comparison to the D) shrunk ovary of the MPA-treated cat.

Histopathological alterations of MPA on the ovarian structure

The ovary of a cat from the treatment group exhibited degenerative changes such as ruptured ovarian wall, including follicular cysts, as observed under a microscope (Figure 5).

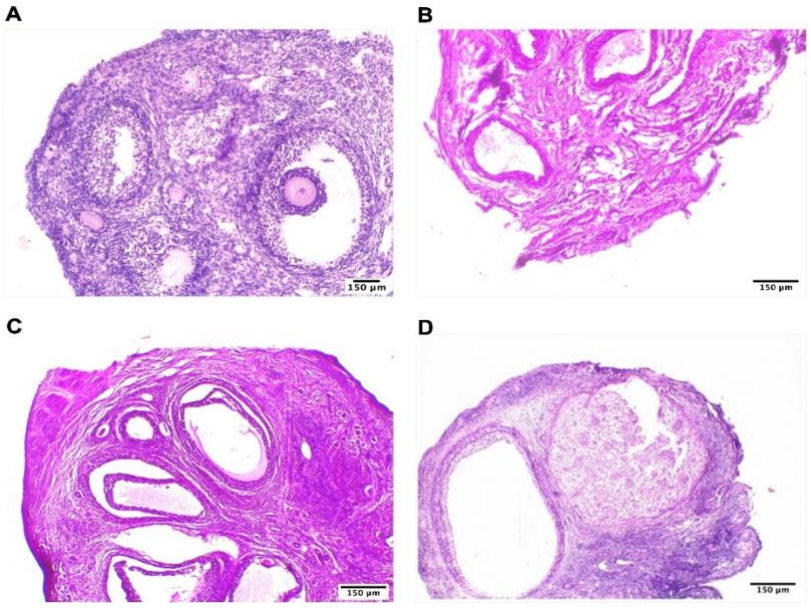

Figure 5. Histopathological findings indicate degenerative changes and follicular cysts in cats from the treatment group. A) shows the normal ovarian structure and normal ovarian wall from the control group (n = 10), and B) illustrates the degenerative changes in the ovary from an MPA-treated cat. C) and D) depict the cystic formations within the ovaries.

There was also one instance of neoplastic change in a female cat's ovary in the treatment group. The histological examination of ovarian tissue revealed abnormalities, and further observation confirmed a diagnosis of liposarcoma, characterised by the presence of adipose tissue (Figure 6).

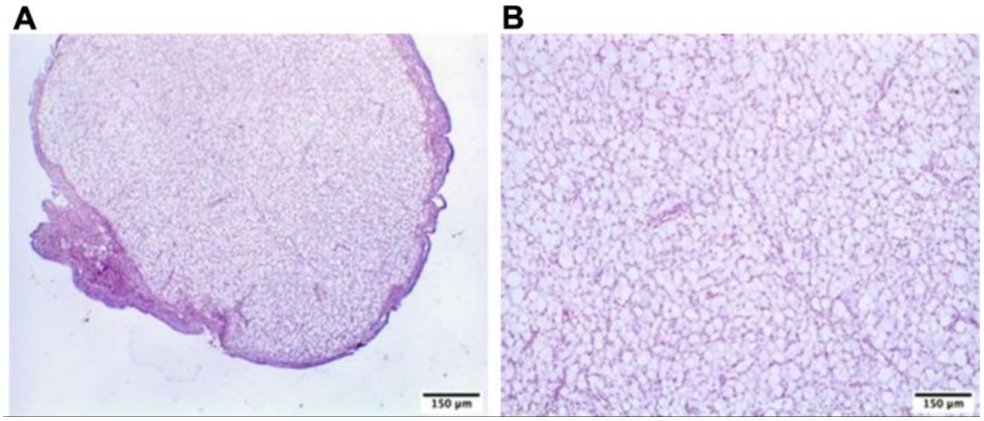

Figure 6. Histopathological examination indicated the existence of liposarcoma in the ovary of a cat in the treatment group. A) showing the overall structure of the ovary (under 4x magnification), and B) showing the presence of adipose tissue (under 10x magnification).

DISCUSSION

MPA is commonly employed among several contraceptive methods to inhibit the estrus cycle in female cats [12]. This study indicates that a dose of 50 mg of MPA is efficient, and it can suppress estrus in cats for a minimum of 42 days.

Prior research indicated that a higher dosage of MPA, ranging from 75 to 100 mg per cat, led to numerous undesirable effects, including cystic ovaries, uterine conditions such as endometritis, cystic endometrial hyperplasia, pyometra, and uterine neoplasms, along with an increased incidence of mammary gland diseases [16,17]. In order to assess the efficacy of MPA as an estrus suppressor and to investigate the potential health risks, this investigation implemented a diminished dosage of 50 mg per cat. The results of this study indicate that a single dose of 50 mg MPA can suppress estrus in cats for a minimum of 42 days.

The average length of estrus in mated female cats, regardless of whether they ovulated or not, was 5.4 ± 0.4 days [23]. The control group also exhibited similar results in the current study. Despite the administration of MPA, two cats in the treatment group showed symptoms of estrus. It may be triggered by environmental factors, such as the presence of three male cats in the same enclosure. The visual, olfactory, and aural presence of an intact male can trigger symptoms of sexual receptivity in female cats [24]. The occurrence of spontaneous ovulation in female cats before introducing a male was between 0-22%; however, it increased to 33-57% when a male was placed in a separate cage inside the same room [25]. The cats in the treatment group displaying indicators of estrus may be nearing the estrus stage of their reproductive cycle; hence, MPA was unable to entirely prevent estrus activities. This indicates that the efficacy of MPA might be affected by environmental factors or the stages of the estrus cycle during MPA administration.

In the current study, the mean length and width of the ovaries in the control group of cats were 0.79 cm and 0.60 cm, respectively. In the treatment group, the length measured 0.66 cm, and the width measured 0.50 cm. According to Gatel & Saunders,

2017, the normal ovaries of female cats measure between 0.68 and 1.5 cm in length [26]. Conze & Wehrend, 2018 stated that the median length of the ovary during anestrus is 0.9 cm in female cats [27]. The administration of MPA can lead to a decrease in ovarian size compared to the typical size of ovaries in rats [28]. Also, the use of MPA induces changes in both the appearance and functionality of the ovaries of albino rats. Consequently, the Graafian follicle of the albino female rat decreases in size [29]. Similar morphological alterations, such as ovarian shrinkage, were also seen in MPA-treated monkeys [30]. The changes in the length and width of the ovaries of the treatment group may be due to the absence of mature follicles on the surface of the ovaries. As there is no folliculogenesis in the ovaries of the treatment group, the length and width are reduced in size.

The shape of a normal cat's ovary is oval [26]. In this study, the MPA-treated group had thinner and smaller ovaries, and this may be due to cessation of folliculogenesis and shrinkage of the ovaries. After MPA administration, the ovary could become thinner than the control group, and the shape could be referred to as flat, as the cortex might be significantly shrunk [28]. A significant reduction in the size of rat ovaries was observed following treatment with MPA [31]. Xenobiotics, whether naturally occurring or artificially produced, such as MPA, can reduce the number of follicles in the ovaries, resulting in a decline in ovarian cells, including oogonia, oocytes, and somatic cells [32]. The histological examination of the ovaries in the females who received depot medroxyprogesterone acetate (DMPA) treatment revealed follicular degeneration and atresia. Apoptosis has been identified as the fundamental process of degeneration [33,34]. MPA administration can cause accumulation of superoxide radicals in the ovaries, which can cause ovarian morphological changes such as reduced size and altered shape [35,36].

Cysts were present in 3 cases among the 10 female cats in the treatment group. The use of synthetic progestins can prevent the luteinizing hormone (LH) surge required for ovulation during the estrus cycle and lead to the development of follicular cysts [37]. Our observations of cyst formation align with Abdelgalil (2023), who also recorded cystic changes after a single MPA administration in female cats [16]. Although Keskin et al. (2009) described pathological outcomes after long-term MPA use, this study shows that even a single dose can cause follicular cysts and degenerative changes in the ovaries [38]. Infertility might result from a higher quantity of cystic ovarian follicles and a higher quantity of dysfunctional ovarian follicles [29]. MPA causes suppression in LH surge, which can lead to improper ovulation and ultimately the formation of multiple pathological ovarian cysts.

Liposarcoma is a prevalent noncancerous tumor that can develop in many parts of the body. However, there is no recorded case of feline ovarian liposarcoma in cats. The causal relationship between MPA and neoplastic development in the ovary cannot be definitively established, as it might also be attributed to any underlying health conditions in the cat. Keskin *et al.*, 2009, suggested that prolonged administration of MPA over a long period might result in the formation of cancerous mammary tumors, inflammation of the uterus, pyometra, and the presence of fluid-filled sacs in the ovaries (ovarian cysts) [38]. Three male housemate cats were subjected to a trial where they received several injections of MPA to address issues of inter-cat aggressiveness and urine home soiling. All three cats later developed mammary adenocarcinomas [18]. Moreover, toxicological investigations have demonstrated that administering large doses (240 mg) of MPA significantly elevates the likelihood of developing breast cancers in female beagle dogs [35]. Animal tests have shown that the injection of progesterone or its synthetic counterparts increases susceptibility to cancers induced by

Rous sarcoma virus and several chemical carcinogens [39]. Although in this study, a liposarcoma was detected in one treated cat, the causal link to MPA administration remains uncertain.

At a dosage of 50 mg, MPA successfully suppressed estrus in 8 cats from the treatment group. All ovaries in the treatment group exhibited morphological changes. The treatment group displayed ovarian shrinkage and a flattened oval shape, resulting in smaller ovaries compared to the control group. None of the 10 control cats had ovarian cysts, whereas the number of female cats having ovarian cysts in the treatment group was 3.

This study was not beyond any limitations. The main limitation was the lack of facilities to perform vaginal cytology before MPA administration. This would have helped to identify the stage of estrus before MPA administration and its consequences in different stages. A hormonal profile analysis after MPA administration would have been useful to track the changes in progesterone levels in the cat's body. A further restriction was the limited sample size. However, managing cats under such conditions (age, sex, previous breeding record, etc.) was challenging, and the available housing space allowed us to accommodate just 20 cats. Despite the constraints, this study will assist future researchers in the discipline of MPA-mediated feline contraception by providing initial morphological and histopathological observations about the effects of MPA on cat ovaries.

CONCLUSIONS

Hormonal contraception remains a common approach for regulating reproduction in domestic cats, with MPA being one of the most often utilised feline contraceptives. This study indicates that a single intramuscular dose of 50 mg MPA appears to suppress estrus for up to 42 days in most cats. The study also suggests that the suppression of estrus depends on environmental conditions and the specific stage of estrus at which the medication is administered. However, associated adverse ovarian changes, including follicular cysts and morphological degeneration observed in this study, warrant further investigation, particularly concerning long-term safety and lower dosage efficacy.

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AUTHOR CONTRIBUTIONS

MTRL and MAR designed outlines and drafted the manuscript. MTRL, RSS, and MTR performed the experiments and analyzed the data. MTRL, MAR, and MS wrote the initial draft of the manuscript. SP, MAAM, ZCD, and ANMAR reviewed the manuscript and the scientific contents described in the manuscript. All authors read and approved the final submitted version of the manuscript.

CONFLICTS OF INTEREST

There is no conflict of interest among the authors.

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