

THE EFFECT OF INTRAUTERINE DEVICE (IUD) ADMINISTRATION ON FERTILITY, SERUM PROGESTERONE, OSTRADIOL 17 BETA AND UTERINE ENDOMETRIUM DURING THE INDUCED ESTRUS CYCLE IN THE BITCH*

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ABSTRACT

In the present study Copper T type intrauterine device (IUD) were inserted to bitches in order to investigate the effects of IUD on fertility, endometrium and serum progesterone and oestradiol 17 beta during the induced oestrus cycle. IUD's were inserted to 10 bitches by surgically and the other 10 bitches served as control without IUD. Every bitch received 0.1ml/kg Cabergoline for eleven days after 3 months. Oestrus cycles of 8 bitches in the treatment and 6 bitches in the control could be induced. Duration of proestrus and oestrus were not different significantly between the treatment and control groups. Bitches had oestrus cycle, were mated but no pregnancy was achieved. Blood samples were collected during the cycle, serum oestradiol 17 beta levels were higher but serum progesterone levels were lower than the control group in proestrus ($P < 0.05$). Three of 8 bitches having IUD's and induced cycles, dropped the IUD's. The uteri of 7 bitches were taken out by ovario-hysterectomy after 15 days. Bloody fluid collection was observed in cornua bearing IUD. The resting bitches were operated and uteri were taken on 25th day, in the cornua bearing IUD was bloody fluid collection and also thickening of the cornual walls. At histo-pathological examinations of these uteri, chronic metritis and pyometra were diagnosed. Insertion of Copper T type IUD's in bitches caused antifertility and this effect was more probably due to serious endometrial changes caused by the local irritation of the device than hormonal effects.

Key words: Bitch, intra uterine device (IUD), fertility.

INTRODUCTION

Contraception, contrary to sterility, is the prevention of pregnancy temporarily. The contraceptives widely used in humans, such as oral steroids, condom, diaphragm, spermicid gel and foam are hard to use in animals and this situation decreases the number of choices (19).

Grafenberg was the first to place a metal ring into uterus for contraception in 1928. In early 1960's the use of plastic intrauterine devices (IUD) in humans and other mammals, and their satisfactory contraceptive effects accelerated the studies (1,2,5,11,13). Recently, approximately 40 million women in China and total 55-60 million women world wide use IUD (19).

There is agreement among researchers that the effect of IUD's is in tubas, ovaries and uterus instead of being systemic (16,17,18). There are several suggestions about the contraceptive effect of IUD's. IUD's are believed to increase the motility of tuba uterina, so ova and blastocytes are expelled from oviduct, shortens the duration of corpus luteum and stops the secretion of progesterone, decreases the cornification of endometrium which is necessary for

implantation, makes a foreign material effect and causes an aseptic inflammation with an ova-toxic environment in uterus (4,7,8,12,21.).

In studies about the effect of IUD'S on ovarian functions in sheep, goat, cattle and pigs, it is found that IUD's have systemic effect, they increase prostaglandin secretion and limits the duration of corpus luteum, this shortens the estrus period also stops the secretion of progesterone necessary for implantation but it does not avoid ovulation (4,17,18). Hawk and Conley (9), reported IUD's stop mechanically spermatozoas passage through cervix.

In this study, Copper T type IUD's which are widely used in women were administered to bitches to investigate their contraceptive action and their effects on endometrium, serum progesterone and oestradiol 17 beta levels during induced estrus cycle.

MATERIAL AND METHOD

20 bitches of various breeds at puberty and 20-30 kg live-weight each were used. 3 male dogs were also used for inseminations.

Administration of IUD's:

IUD's were administered to 10 bitches by laparoscopy. Cornua uteri were taken out through a 2-2.5cm incision from fossa paralumbales. According to the width of cornua the sides of IUD's were shortened and placed one into each cornua.

Induction of Cycles :

In 3 month after the administration of IUD's the cycles of bitches were controlled by vaginal cytology (10,20) and 20 bitches at anestrus were treated with daily 0,1 ml/kg Cabergolin (Galastop, Vetem S.P.A.) for 11 days orally to induce oestrus. Bitches on oestrus were inseminated artificially on 1st, 3rd and 5th day of oestrus.

Control of Uteri and Ovari:

The oviducts and uteri of 4 bitches in the treatment group and 3 in the control group which had oestrus and inseminated, were flushed and embryos were controlled. All bitches were ovario-hysterectomised. Presence of corpus luteum were controlled on ovaries and uteri were sent to laboratory for histopathological controls on 15th day post inseminations. For the control of nidation, 4 bitches from the treatment and 3 from the control were ovariohysterectomized on 30th day post inseminations. Corpus luteum were controlled and uteri were sent to histopathological evaluations.

Histopathological Examinations:

After ovariohysterectomy operations, uteri were fixated in %10 formal saline. Fixed uterus parts underwent routine preparation manipulations (14). These preparations were stained in hematoxylin-eosin (H.E.) and examined under light microscope.

Sampling and Manipulations:

Vaginal smears and blood samples were taken from the day before Cabergolin treatment (0.day) to the end of inseminations. Vaginal smears were stained with Papanicolaou staining technique and evaluated according to classical methods (10,20).

Blood sera were kept -20°C until hormone evaluations. Hormone level were determined by radioimmunoassay at the end of the study (3,20).

RESULTS:

Sexual cycles could be induced in 6 control and 8 treatment bitches (70%) with Cabergolin treatments (Table 1). No significant difference was observed between the proestrus and oestrus periods of treatment and control bitches (Table 2). According to hormone profiles, oestradiol level of the treatment group during proestrus was higher (Fig.1) but serum progesterone level was lower than the control group (Fig.2).

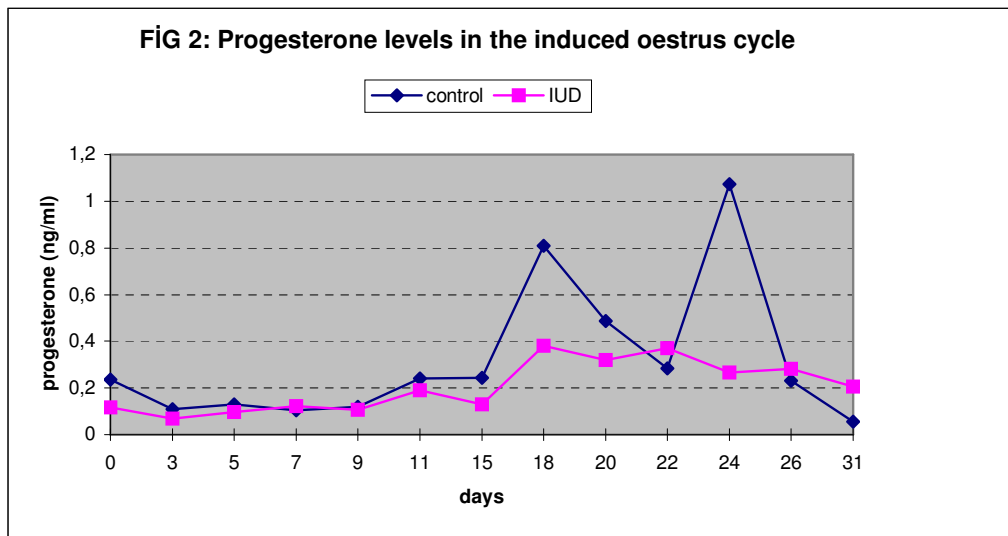
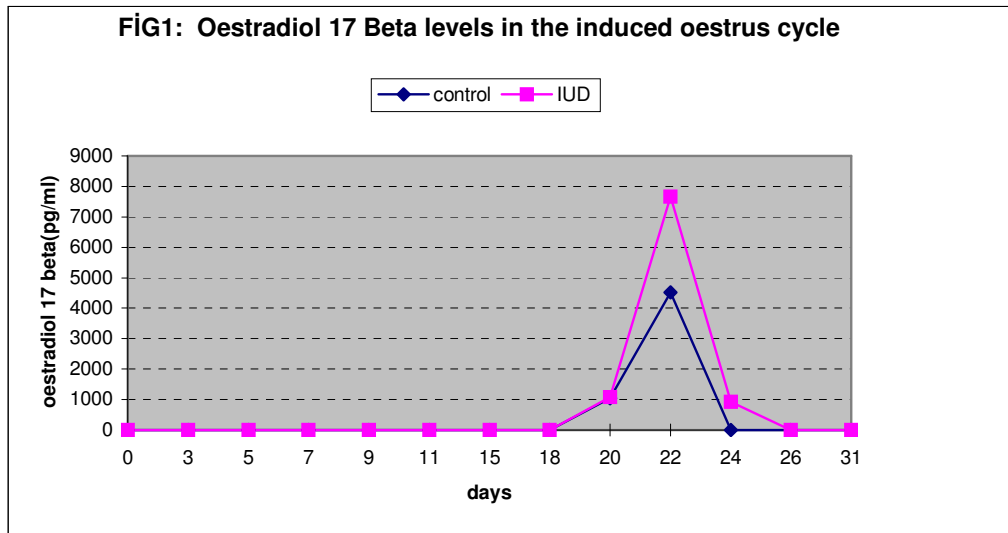
Table 1: Induced oestrus cycle according to vaginal smear.

Days	0	3	5	7	9	11	14	16	18	20	22	24	26	31	35
Control															
101	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2
102	1	1	1	1	1	2	2	2	2	4	4	4	4	4	4
138	1	1	1	1	1	2	2	2	2	3	3	3	4	4	4
134	1	1	1	1	1	2	2	2	2	2	2	2	2	2	2
118	1	1	1	1	1	1	1	1	1	2	2	2	3	3	3
139	1	1	1	1	2	2	2	2	2	3	3	3	3	4	4
IUD.															
205	1	1	1	1	1	2	2	2	2	2	2	2	4	4	4
204	1	1	1	1	1	2	2	2	2	2	2	2	3	3	3
202	1	1	1	1	1	2	2	2	2	2	2	2	3	3	4
11	1	1	1	1	1	1	1	1	2	2	2	2	3	3	3
10	1	1	1	1	1	2	2	2	2	2	4	4	4	4	4
201	1	1	1	1	1	2	2	2	2	2	3	3	4	4	4
212	1	1	1	1	1	2	2	2	2	2	2	4	4	4	4
203	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2

1: Anoestrus 2: Proestrus 3: Oestrus 4: Metoestrus

Table 2: Duration of proestrus and oestrus in the induced oestrus cycle.

Group	Duration of Proöstrus (day)	Duration of oestrus (day)
IUD inserted	11.87 ± 4.45	3.12 ± 4.01
Kontrol	11.33 ± 7.6	3.16 ± 3.8



Findings of ovariectomy on the 15th day after inseminations were shown Table 3. 2 of the bitches induced oestrus, dropped their IUD's. No embryo or ova were observed at the flushing of oviducts and uteri, although observed corpus luteum on ovaries on the 15th day after inseminations. Bloody fluid and thickening of cornual walls was observed in the IUD's containing cornua. When these uteri were examined histopathologically, almost all lamina epithelialis of uterine mucosa seemed to scatter and most of the uterine glands in propria mucosa to disappear. Also severe cellular infiltration of few leukocytes, so many lenfocytes, plasma cells and mononuclear macrophage was observed. In some sections this cellular

infiltration was replaced by fibrous proliferations. Mucoid masses with leucocytes intensity were observed in the lumen of uteri (Fig 3).

Findings of ovariectomy on the 30th day after inseminations were shown Table 4. No pregnancy was observed both of the groups. One of the bitches induced oestrus dropped her IUD and chronic endometritis and pyometra (only one bitch) were observed in the uteri had IUD, on the 30th day after inseminations. Histopathological examinations of these uteri, endometrial proliferations were observed. In sections with endometrial proliferations, obvious hyperplasia and hyperplastic epithelial cells forming papillae towards the lumen were observed. Mucoid masses containing neutrophil leucocytes and scattered epithelial cells was observed in the lumen. In the propria mucosa, number of the uterine glands were increased and some of them were in cystic form. Also, hyperemic vessels and mononuclear macrophage, plasma cell leucocyte and leucocyte cell infiltrations with obvious fibrous proliferations were observed in propria mucosa (Fig. 4).

The bitches whose estrus cycles couldn't be induced were excepted from the study and their hormone and histopathological examinations were not evaluated. Hormone level of 3 bitches which dropped their IUD's were also not considered.

DISCUSSION:

It is observed that IUD's achieve good antifertility results in bitches like other domestic animals and humans. Unlike Chander and Gupta (4) reports no adverse effect on oestrus induction were seen. In 8 of 10 IUD administered bitches, oestrus cycles could be induced. In blood samples collected every other day from bitches with IUD's during induced cycle, progesterone level was observed lower and oestradiol level higher. This can be a result of enhanced prostaglandin secretion from endometrium by IUD's as reported by some researchers (18,4,21). These findings support the reports of some researchers (17,6) suggesting IUD's stop the effect of progesterone which is necessary for implantation and cause a contraceptive effect.

IUD's are reported to interfere cornification of endometrium for nidation and prevent embryos nidation (18) In our study, at the histopathological control of uteri on the 15th day after inseminations, the lamina epithelial layer of mucosa was scattered totally. Also, there was an aseptic inflammation liquid in the lumen and cellular infiltration composed of few leucocytes and so much macrophage confirming the results of some workers (19,8,7). These inflammation products make an unsuitable environment to spermatozoa and decrease their numbers in oviduct (7,9).

Contrary to the studies in rabbits and monkeys (6), no embryo could be recovered in uterus and oviduct flushing when corpus luteum were observed on ovaries (Table 3).

Table 3 : Findings of ovariectomy on the 15th day after inseminations.

IUD	Bitch No:	Ovarium		Uterus
		Right(C.L)	Left(C.L)	
	10	2	2	IUD(-) Uterus normal
	201	2	1	IUD(+) Bloody fluid in the cornua lumen
	212	5	1	IUD(-)
	203	2	3	IUD(+) Bloody fluid in the cornua lumen
CONTROL	134	4	5	Uterus normal
	118	5	7	Uterus normal
	139	4	3	Uterus normal

At histopathological investigations of uteri taken on 30th days after inseminations, endometritis and in one bitch pyometra were observed in IUD containing cornua. The incidence of pelvic inflammatory disease is increased in women inserted IUD's. If the patient is free from infection when the IUD is inserted, the risk of developing a related pelvic inflammatory disease is about 3 times that of the control population (19,2). However, in bitches which dropped their IUD's there were no inflammation in uteri. These findings showed, inflammations caused by IUD's are reversible. This is a good example to the thought that the cellular exudate collected in IUD containing cornua as a result of chronic inflammation, makes an embriotoxic and nidation preventing effect (15,19,6). From 3 of 8 IUD administrated and oestrus induced bitches, IUD's were dropped. This shows that IUD's dropping rate is high in humans during the first month of administration (19).

IUD's were effective in contraception in bitches, meantime although reversible, they can cause chronic endometritis and pyometra. We concluded that IUD's contraceptive effect in bitches partially hormonal but mostly as a result of local irritation and severe endometrial differences.

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Table 4: Findings of ovariectomy on the 30th day after inseminations.

	Bitch No:	Ovarium		Uterus
		Right(C.L)	Left(C.L)	
IUD	205	2	2	IUD (-) Uterus normal.
	204	-	2	IUD(+) Bloody fluid in the cornua
	202	3	-	IUD(+) Thickening of cornual walls, cystic endometrium and bloody fluid.
	11	3	1	IUD(+)
CONTROL	101	-	-	Uterus normal
	102	1	-	Uterus normal
	138	-	-	Uterus normal

FIG.3: Inflammatory cell infiltration in mucosa, exudate collection in the lumen (H.E.100X).

FIG.4: Increase in the number of uterine glands and cell infiltration in interglandular spaces. Hiperplasia in L.epithelialis, exudate rich in leucocytes collected in the lumen (H.E. 100X).