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IMPROVING FERTILITY OF THE FEMALE RABBITS

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INTRODUCTION

Rabbits could be considered one of the main sources of meat that would cover a part of meat needed for human consumption. Rabbit breeders are, sometimes faced by infertility or lowered fertility for which the does may be responsible due to anovulation or decreased number of ova shed (Hafez, 1970).

Ovulation and superovulation are of great importance in rabbits and provide a potential means of improving litter size (Espey, 1982). Therefore this investigation was carried out to test the effect of treatment with some new drugs namly Prostaglandins, Clomid and Gonadoreline in inducing ovulation in the infertile rabbits.

MATERIALS AND METHODS

The present experiment was carried out on 60 infertile cross-bred rabbits (Baladi with different standard breeds (Bauscatt, chenchille and Flander). The animals were chosen during season 1984 from the rabbits flock of the poultry Research Center of Alexandria University. The records of these animals during the first and the second breeding seasons showed infertility or temporary stlrility causing their inability to produce viable youngs.

The animals were divided at random into six groups of ten does each. Five of the six groups were put under five different treatments and the last was left as a control as shown in Table (1). The experiment continued for five consecutive deliveries repeating the treatment before mating every delivary.

Animals were housed in individual cages and fed on a concentrate mixture consisting of 50% barley, 20% yellowcorn, 15% decorticated cottonseed meal, 5% horse-bean, 7.5% fich meal (C.P. 40%), 1% lime stone, 0.5% bone meal and 1% mixture of minerals and vitamins. During winter, animals were fed on Berseem (Trifolium alexndrinum) in addition to the concentrate ration. (Feed and fresh water were provided ad libitum.)

During the experimental period, measurements were carried out on each doe in each group for number of kindlings, conception rate (C.R), gestation period, mortality at day of birth, and at 21 days after birth, body weight at day 21 of age and total meat production in different delivery sequences and treatments.

Table 1: The six experimental groups of rabbits and the doses of hormones used in each treatment.

Group	Hormones used	Dose
I	Untreated (control)	-
II	¥ Estrumate ($PGF_2\alpha$)	100 ug/Rabbit
III	¥ $PGF_2\alpha$ + Gonadorline	+
IV	¥¥ Clomid	12.5 mg/Rabbit
V	Clomid + Gonadorline	+
VI	¥¥¥ Gonadorline	.05 mg/Rabbit

¥ Estrumate (ICI) is a synthetic prostaglandin analogue related to ($PGF_2\alpha$). Each ml contains 263 ug of cloprostenol sodium equivalent to 250 ug of cloprostenol.

¥¥ Clomid (Merrell) clomifene citrate.

¥¥¥ Gonadoreline (Hoechest) containing synthetic releasing hormone for both the luteinising and follicle-stimulating hormones (GnRH). Each ml contains 0.05 mg gonadoreline.

+ Combination of doses were made as indicated in table for each single drug.

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RESULTS AND DISCURSION

1. Reproductive Performance:

1.1 Conception rate:

The average conception rate in the six studied groups were 36, 64, 54, 46, 42 and 44% in control, prostaglandin, prostaglandin + Gonadoreline, Clomid, Clomid +Gonadoreline and Gonadoreline treated groups respectively. These results indicate that prostaglandin treatment had the highest effect on the conception rate followed by $PGF_{2\alpha}$ + G,C, G then the C + G treatment coming last. The animals were responsive to all hormonal treatments during the whole experimental period, suggesting that repeated treatment had no bad effect on conception rate. The effect of delivary sequence on C.R. was not as marked as that of treatment. Conception rates in the first to the fifth delivary sequences were 50, 46.7, 51.7, 50 and 45% respectively. The overall mean was 47.7

1.2 Gestation period:

The overall mean of the gestation period for all animals was 30.22 day. Irrespective of deliveries the average gestation period for the control, $PGF_{2\alpha}$, $PGF_{2\alpha}$ + G, C, C + G and G were 30.50, 30.25, 30.04, 30.26, 30.19 and 30.14. Irrespective of the treatment the averages of gestation periods in the first, second, third, fourth and fifth deliveries were 30.27, 30.20, 30.26, 30.10 and 30.26 respectively. Neither hormonal treatment nor litter sequence had any significant effect on the gestation period.

In the present study the gestation period ranged from 30.04 to 30.5 days. Differences in gestation period was correlated with litter size since the longest gestation period 30.5 days was in the control group which had a litter size about 3.6 youngs while the shortest gestation period 30.04 was found in animals treated with Prostaglandin plus Gonadoreline which had a litter size about 7.3 youngs. This decrease in gestation period with increasing litter size is in agreement with the results of Wilson and Dudley (1965), and Sandford (1979)who reported that gestation period generally ranges from 31-32 days and is affected by the time of year, the size of the doe and litter size.

1.3. Litter size:

Results in Table 2 indicate that the mean litter size was greatest in the 4th delivery (6.53) followed

by the 2nd (6.36), the 3rd (6.1), the 5th (5.48) and finally by the 1st delivery (4.87). Animals treated with PGF2α had the greatest mean litter size (7,84) followed by those treated with prostaglandin plus Gonadoreline (7.33), The lowest mean litter size was found in the untreated control group, (3.56). Hormonal treatment and delivery sequence both had significant effect ($p<.01$) on litter size.

In the present study no significant differences were detected between litter size or conception rate (C.R.) in groups of animals treated with Clomid or Clomid plus Gonadoreline. These results are in agreement with those of Kistner (1966); Schally et al., (1970); and Jewelewicz (1975). Rabbits treated with Clomid and Clomid plus Gonadoreline have C.R.and litter size higher than those of the control group but lower than rabbits treated by prostaglandin or prostaglandin plus Gonadoreline. These results are in agreement with Ruiz Velasco (1979) who reprted that ovulation was induced in 70% of anovulatory cases treated with clomiphene. However, the pregnancy rate was significantly in the lower range (from 27-40%). On the other, hand, Davidson et al. (1965) reported that clomiphene compounds with oestrogenic activity inhibited fertility in female rats.

The means litter size and C.R.were 4.59 and 44% in the group of animals treated with Gonadoreline (synthetic LH-RH), which were higher than those in the control group This drug is known to increase LH secretion.

1.4. Mortality and viability:

The number of offsprings that died in the 1st day and during the 1st three weeks of age and the mortality rate in the six studied groups are shown in Table 3.Mortality rates were relatively high during the 1st day and 1 st week, then decreased in the 2nd and 3rd weeks in all groups.

Over the3 weeks period the mortality rate was highest (39.8%) in the prostaglandin-treated group and lowest(18.8%) in the Gonadoreline treated group. The high rates of mortality in prostaglandin and in the prostaglandin plus Gonadoreline-treated groups may be due to larger litter size and to the higher mortality at the 1st day after delivery due to lower birth weights and competition for mother's milk. Thus could be correded by using foster mathe syslem.

Broeck et al.(1976) showed that the mortality was highest in very small (less than 5) and in very large litters (more than 13). Rao et al.(1977) also found significant relationship between litter size and mortality.Results in Table 3 indicated that the total average mortality percent tended to decline as the animals progressed in age regardless of treatment and that the mortality at the day of delivery was higher in animals giving high litter size.

2. Body Weights at 21 Days of Age:

2.1. Mean body weight:

Table 4 shows the mean body weights at 21 days of age in the six studied rabbit groups in the different sequences of delivery. Analysis of variance showed that body weights were significantly affected ($p<0.01$) by treatment but not by delivery sequence. Regardless of the sequence of delivery, the mean body weight of the youngs were heaviest (282 mg) in the control group and lightest (234 mg) in the prostaglandin plus Gonadoreline group.

2.2 Mean Litter weight:

Table 5 presents mean litter weights at 21 days of age for the six rabbit groups in the different sequences of delivery. Analysis of variance showed that litter weight was significantly affected by treatment ($p<0.01$) and by litter sequence ($p<0.05$).Regardless of the sequence of delivery, the mean litter weight was highest (1.20kg) in the prostaglandin-treated group and lowest (0.813 kg) in the control group. Regardless of treatment,litter weight was highest ($p<0.05$) in the 4th sequence of delivery (1.130 kg). Litter weights in other delivery sequencies were not significantly different from each other but showed a gradual increase from the 1st litter up to the 4th followed by a decline in the 5th litter (Table 5).

2.3. Total live body weight:

Table 6 indicates that the total live body weight of the youngs at 21 days of age were highest in the prostaglandin-treated group (36.12 kg) than in any other group. Generally, hormonal treatment increased the total meat produced at 21 days of age than that from the control group. The mean total live body weight produced by the treated groups was 26.37 kg. compared to 13.83 kg. poduced by the untreated group.A general trend denoting an increase in total live body weight was observed from the 1st to the 4th delivary followed by a marked decrease in the fifth.

GENERAL DISCUSSION

1. Prostaglandin treatment :

All drugs used increased litter size significantly. but the increase caused by prostaglandin treatment was the highest. These results are in agreement with those of many investigators, who indicated that $PGF_{2\alpha}$ is among the better treatments for increasing ovulation rate detected

by litter size (Grinwich et al., 1972. Ainsworth et al., 1975; and Espey, 1982). These initial findings were confirmed in other species, inculuding mice (lau et al.,1974), rabbits (Grinwich et al., 1972) and pigs (Ainsworth et al., 1979).

Moreover injection of antiserum against PGs systemically (Lau et al.,1974) or intrafollicularly (Armstrong et al.,1974) blocked the LH-induced ovulation in oestrous rabbits. These results are additional support to the concept of a significant role of PGs in ovulation and confirmed the suggestion of Kohda et al.,(1983) that PGs mediated the action of LH on ovulation.

Evidence for the role of PGs at the follicular level was provided by the findings that intrafollicular levels of PGs of both E and F series increased markedly shortly before ovulation (Yang et al.,1974; Ainsworth et al.,1975; Tsang et al.,1979; Brown and Poyser, 1984). Both PGF and PGF metabolites showed a lineer increase with time and number of ovulations (Schalff et al.,1983; Brown and Poyser, 1984). Therefore the average PG content could be related to the number of ovulations and ovulatory efficiency, but not to the total number of follicles. It is of interest to note from studies on rabbits (Yang, 1974; Phi et al.,1977; Ainsworth et al., 1979; Armstrong, 1981) that PGE level remained elevated somewhat longer than PGF level after ovulation leading to the suggestion that, while PGF may be most important for follicular rupture, PGE may play some role in the luteinization process which normally follows ovulation.

Prostaglandin action as luteolytic agent is clear in the present study since most of the animals used in this study may had been suffering from cystic corpus luteum causing infertility or at least lowered fertility.However the prostaglandin treatment was more effective on most of the studied parameters. The results of many investigators indicated that an important effect of prostaglandins is their action as luteolytic agents in rabbits when administered in large, supra-physiological doses (Scott and Rennie, 1970; Gutknecht et al.,1972; and Bruce and Hillier, 1974).

Treatment with Clomid or with Clomid plus Gonadoreline were not significantly different from Gonadorline alone. However, these treatments had significant effect on litter size compared with the cotrol. This suggests that Clomid and similar drugs can cure infertility or lowered fertility through increasing ovulation rate. Previous findings of

Ruiz Velasco (1979) showed that Clomiphene caused high ovulation rate accompanied by lower pregnancy rate and a 14% abortion rate. Jewelewicz (1975) and Ruiz velasco (1979) classified the cases which have a good chance to respond to clomiphene when the level of oestrogen and gonadotrophins are within the normal range as polycystic ovaries, oligoovulation and anovulation.

Ruiz velasco (1979) suggested that clomiphene should be used in sterile cases which lack ovulation due to hypothalamic dysfunction only when the ovaries, the pituitary and the hypothalamus can be made to function normally. Moreover, production of oestrogenic and gonadotrophin hormones levels must be adequate (neither too high nor too low). Kistner (1966) reffered to the cases which did not respond to clomiphene as those with extremely high or extremely low total gonadotrophins, and those cases having premature ovarian failure in which the gonadotrophins are very low or very high and oestrogen is undetectable.

On the other hand McPherson et al.,(1977) reported that serum LH levels were significantly increased above control levels 10 minutes after the administration of 10ng LH-RH and its levels continued to increase with increasing dosage of LH-RH up to 40 and 80 ng. LH was considered as the factor which caused regression of CL (Scott and Rennie, 1970). The effect of LH was dose-dependent where doses of 15 ng and higher caused ovulation and luteal regression. While doses of 5 and 10 ng faild to cause luteal regression and ovulation was seen only in some of the rabbits (Scott and Rennie, 1970).

In conclusion, the drugs used in this study caused an increase in ovulation rate and fertility of rabbits. The animals differed in their response according to the cause of infertility, and some animals did not respond to the treatment, One reason could be that superovulation reduced the number of implants (Hafez, 1970). Also in superovulation , most embryos are resorbed after implantation Adams, (1960). Accordingly, embryo recovery and fertilization rate are decreased as the number of ovulation increased (Varian et al.,1967; MizoGuchi and Dukelow,1981).

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SUMMARY

The aim of the present investigation was to study the effect of 5 different drugs (hormones or hormonélike substances) in improving fertility of female rabbits. Sixty infertile female cross- bred rabbits (Baladi with different standard breeds) were divided randomly into six groups of then dœs each.

The study included five successive deliveries.. Reproductive performance of the does were recorded; conception rate, gestation period, and litter size. Other measurments were also obtained on the offsprings such as mortality, viability, litter weight at 21 days of age, individual body weight and the total live body weight of younges at 21 days of age.

Results on the does and their offsprings suggested that hormonal treatments in general increased the conception rate, litter size and total meat production from the infertile does. No sid-effects were noted on the doe or its youngs by repeating the treatment.

Present results suggest that treatment with $PGF_{2}\alpha$ and with $PGF_{2}\alpha$ plus Gonadorelin (G) gave the best improvement in conception rate, litter size and meat production, since difference between $PGF_{2}\alpha$ and $PGF_{2}\alpha$ plus G were not significant. The use of $PGF_{2}\alpha$ alone is recommended. The present results clearly showed that infertility cases under Egyptian farm conditions were due to the spread of cystic C.L. and to pseudopregnancy. For this reason the effectiveness of prostaglandin treatment was very high. The rise in mortality rate following this treatment could be corrected by the use of foster mothers with large litter size does.

Teble (2) : Mean litter size at birth for the six studied rabbit groups through five delivery sequences.

Treatment	Mean litter size ± SE										
	Delivery sequence										Overall
	n	1st	n	2nd	n	3rd	n	4th	n	5th	mean
Control	3	2.33±0.67	4	4.25±0.75	4	3.75±0.48	3	4.00±0.58	4	3.25±0.25	3.56 ± 0.27^{c}
$PGF_{2\alpha}$	6	6.50±1.06	7	8.71±0.42	7	7.57±0.10	6	8.00±0.37	6	8.33±0.49	7.84 ± 0.34^{a}
$PGF_{2\alpha}$ + G	5	6.80±1.02	4	7.75±0.75	7	6.86±0.83	7	8.43±0.69	4	6.50±0.87	7.33 ± 0.38^{a}
C	5	4.40±0.75	3	6.00±0.58	5	5.60±0.51	7	5.43±0.61	3	5.00±1.50	5.26 ± 0.33^{b}
C + G	5	4.00±0.63	5	4.60±0.68	5	5.00±0.63	2	7.50±1.50	4	5.00±1.08	4.91 ± 0.38^{b}
G	6	4.00±0.37	2	4.50±1.50	3	6.67±0.88	5	4.80±0.73	6	4.00±0.77	4.59 ± 0.36^{b}
Overall mean		4.87 ± 0.89^{a}		6.36 ± 0.45^{bc}		6.10 ± 0.39^{bc}		6.53 ± 0.40^{c}		5.48 ± 0.46^{ab}	5.86±0.19

Within raws or columns, any two means having at least one letter in common do not differ significantly ($P \leq 0.05$)

Table (3): Mortality and mortality rates in the six studied rabbit groups.

Treatment	No. of offsprings		Mortality				Total
			1st day	1st week	2nd week	3rd week	
Control	64	N	2	7	4	2	13
		%	3.1	10.9	7.0	3.8	20.3
Prosta glandin (PG)	251	N	48	72	20	8	100
		%	19.1	28.7	11.2	5.0	39.8
PG+Gonadoreline (G)	198	N	28	46	15	7	68
		%	14.1	23.2	9.9	5.1	34.3
Clomid (C)	121	N	5	17	6	5	28
		%	4.1	14.1	5.8	5.1	23.1
C + G	103	N	3	14	5	3	22
		%	2.9	13.6	5.6	3.6	21.4
Gonadoreline (G)	101	N	4	12	4	3	19
		%	4.0	11.9	4.5	3.5	18.8
Total	838	N	90	168	54	28	250
		%	10.7	20.0	8.0	4.5	29.8

Table (4): Mean body weight at 21 days of age for the younge in the six studied rabbit groups through five delivery sequences.

Treatment	Mean body weight ± SE (kg)										Overall Mean	
	Delivery sequence											
	N	1st	N	2nd	N	3rd	N	4th	N	5th	N	
Control	5	0.292±0.017	11	0.297±0.033	13	0.263±0.015	11	0.248±0.007	11	0.306±0.035	51	0.282±0.012[a]
Prostaglandin (PG)	27	0.252±0.012	34	0.229±0.017	25	0.275±0.026	32	0.250±0.01	33	0.225±0.008	151	0.247±0.007[b]
PG + G	25	0.218±0.018	20	0.243±0.007	34	0.242±0.010	33	0.220±0.012	18	0.253±0.013	130	0.234±0.008[b]
Clomid (C)	18	0.249±0.006	13	0.265±0.013	19	0.251±0.004	31	0.255±0.011	11	0.289±0.066	92	0.258±0.009[ab]
C + G	17	0.258±0.008	17	0.266±0.012	21	0.252±0.008	10	0.239±0.01	16	0.282±0.048	81	0.261±0.009[ab]
Gonadoreline (G)	22	0.268±0.010	9	0.243±0.016	14	0.264±0.004	19	0.278±0.034	18	0.312±0.032	82	0.279±0.012[a]
Overall mean	114	0.253±0.006	104	0.256±0.008	126	0.257±0.006	136	0.249±0.008	107	0.276±0.014	587	0.258±0.004

N : Total number of younge at 21 days of age .

Any two means having at least one letter in common do not differ significantly (P < 0.05).

Table 5: Mean litter weight at 21 days of age for the young in the six studied rabbit groups through five delivery sequences.

Treatment	Mean litter weight ± SE (Kg)										Overall mean
	Sequence of delivery										
	N	1st	N	2nd	N	3rd	N	4th	N	5th	N	
Control	2	0.772±0.118	4	0.755±0.125	4	0.845±0.032	3	0.907±0.066	4	0.815±0.013	17	0.813±0.031^{C}
Prostaglandin $F_{2\alpha}$	6	1.117±0.085	6	1.283±0.067	6	1.068±0.161	6	1.325±0.083	6	1.227±0.079	30	1.204±0.042^{A}
Prostaglandin + G	5	1.053±0.073	4	1.205±0.159	7	1.160±0.061	6	1.199±0.112	4	1.125±0.147	26	1.150±0.043^{A}
Clomid (C)	5	0.917±0.093	3	1.122±0.140	5	0.948±0.083	7	1.116±0.077	3	0.957±0.122	23	1.016±0.039^{B}
Clomid + Gonadoreline	5	0.871±0.044	5	0.886±0.078	5	1.061±0.106	2	1.18 ±0.180	4	1.034±0.096	21	0.980±0.037^{B}
Gonadoreline (G)	6	0.968±0.059	2	1.068±0.293	3	1.233±0.092	5	0.994±0.069	6	0.873±0.068	22	0.993±0.034^{B}
Overall mean	29	0.971±0.035^{b}	24	1.061±0.39^{ab}	30	1.055±0.45^{ab}	29	1.138±0.043^{a}	27	1.013±0.045^{b}	139	1.048±0.021

within rows or columns, any two means having at least one letter in common do not differ significantly ($P < 0.05$).

N = Number of litters obtained from all does at 21 days in each group .

Table (6): The total live body weights of the 21 day old youngs in the six rabbit studied groups through five delivery sequences.

Treatment	Total live body weight (Kg)											
	Delivery sequence											
	N	1st	N	2nd	N	3rd	N	4th	N	5th	N	Total
Control	5	1.445	11	3.020	13	3.380	11	2.720	11	3.260	51	13.825
Prostaglandin (PG)	27	6.700	34	7.695	25	6.410	32	7.955	33	7.360	151	36.120
PG + G	25	5.265	20	4.820	34	8.128	33	7.195	18	4.500	130	29.905
Clomid (C)	18	4.585	13	3.365	19	4.740	31	7.815	11	2.870	92	23.375
C + G	17	4.355	17	4.430	21	5.305	10	2.360	16	4.135	81	20.585
Gonadoreline (G)	22	5.815	9	2.135	14	3.700	19	4.970	18	5.235	82	21.855
Total	114	28.165	104	25.465	126	31.660	136	33.015	107	27.360	587	145.665

N : Total number of youngs at 21 days of age.

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الملخص العربـــــى

أجريت هذه الدراسة بهدف تحسين الخصوبة فى اناث الارانب المنخفضة الخصوبـــة بدراسة تأثير معاملات بأنواع مختلفة من الهرمونات أو مواد شبيهه بالهرمونات على رفع كفائتها التناسلية . أستخدم فى هذه الدراسة ستون أنثى من اناث الارانـــب الخليطة (بين البلدى وبعض السلالات الاجنبية) والتى أظهرت أنخفاض فى الخصوبـــة وعقما مؤقتا وتم تقسيم الحيوانات الى ستة مجاميع متساوية فى العدد (عشرة فـى كل مجموعـــة) .

وكانت معاملاتها كالاتـــى :

مجموعة غير معاملة (كنترول) ، مجموعة معاملة بالبروستاجلاندين ، مجموعة معاملة (بالبروستاجلاندين + جونادورلين) ، مجموعة معاملة بالكلوميد ، مجموعـــة معاملة (بالكلوميد + جونادورلين) ثم مجموعة معاملة بالجونادورلين فقط .

وقد تم أخذ القياسات الاتية لمدة خمس ولادات متعاقبة :

أولا : قياسات على الام مثل معدل الحمل ـ طول فترة الحمل ـ حجم البطن عند الـولادة ـ ناقـق يوم الـــولادة .

ثانيا : قياسات على النتاج مثل النسبة المئوية للناقق عند ٢١ يوم من العمـــــر ـ الحيوية ووزن البطن ـ متوسط وزن الفرد فى البطن واجمالى وزن النتاج فـــى كل معاملة .

النتائج على الامهات والنتاج أظهرت أن المعاملة الهرمونية عموما حسنت كـــلا من معدلات الحمل وحجم البطن وبالتالى كمية اللحم المنتج من هذه الاناث المنخفضـــة الخصوبة . كذلك لم يكن هناك أى آثار جانبية على الاناث أو خلقتهـا بتكرار المعاملة حتى خمس مرات متعاقبة .

وقد أوضحت النتائج أن المعاملة بالبروستاجلاندين منفردا كان له أثرا فعـــالا فى تحسين معدلات الحمل وحجم البطن ولم يكن هناك اختلافات معنوية بينه وبيـــــن استعمال الجونادورلين معـــه .

من هذه الدراسة يتضح أن معظم حالات انخفاض الخصوبة فى الارانب تحت ظـــروف المزارع المصرية قد يرجع لانتشار حالات تحوصل الاجسام الصفراء وأيضا الحمـــــل الكاذب ولهذا السبب كانت المعاملة بالبروستاجلاندين أكثر فاعلية ..

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