BRIEF NOTE

Therapeutic Effects of an Analog of Luteinizing Hormone-Releasing Hormone (Des-Gly¹⁰-LH-RH-Ethylamide) on Cows with Cystic Ovary

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(Received for publication October 25, 1979)

Cystic ovarian disease (COD) associated with infertility is caused by a lack of luteinizing hormone (LH) released in cows [3, 4, 6, 11]. Human chorionic gonadotropin (HCG) having an activity like LH has widely been used for the treatment of COD [9, 11]. Recently, a synthetic LH-releasing hormone (LH-RH) has been introduced for a clinical application to COD in place of HCG [1, 2]. A more potent analog of LH-RH (Des-Gly¹⁰-LH-RH-ethylamide; TAP-031) was synthesized in Japan. It has a biological activity 5 times as high as that of synthetic LH-RH [5].

This paper reports the therapeutic effect of the new analog of LH-RH (TAP-031) on cows with COD, in comparison with that of HCG.

A total of 160 cows with COD derived from commercial dairy farms located in 6 areas of Hokkaido, or the northern part of Japan, were utilized for this study. They have had one or more large unovulatory follicles 2.0 cm or more in diameter remaining in the ovary for at least one week.

The 160 cows were divided into 3 treatment groups, 1, 2 and 3. Of them, 53 cows belonging to group 1 were first injected in-

tramuscularly (i.m.) with 200 µg of TAP-031 (DA-151, Takeda Chemical Industries Co., Ltd., Osaka). About 14 days after this treatment responses of ovaries were examined per rectum. Cows not responding to the treatment were re-treated with 500 µg of TAP-031. The 58 cows of group 2 first received an i.m. injection of 500 µg of TAP-031. This treatment was repeated in cows not responding to the first injection. The 49 cows of group 3 were given an i.m. injection of 10,000 MU of HCG (Puberogen, Sankyo Zoki Co., Ltd., Tokyo, and Gonatropin, Teikoku Hormone Mfg., Co., Ltd., Tokyo). If this treatment was unsuccessful, 400 KE of bovine anterior pituitary gonadotropin (APG) (Hypohorin, Teikoku Hormone Mfg., Co., Ltd., Tokyo) would be injected intravenously.

Age of the cows and interval of time between parturition and treatment averaged 7 ± 3 (S.D.) years and 104 ± 48 days, respectively, in group 1, 7 ± 3 years and 120 ± 59 days in group 2, and 7 ± 2 years and 109 ± 62 days in group 3.

Blood samples were taken via the jugular vein before and 14 days after the first treatment. Serum obtained by centrifugation at

Table 1. Fertility of cows with cystic ovary after treatment with 200 or 500 μ g of an analog of LH-RH (TAP-031), 10,000 MU of HCG, and 400 KE of bovine APG

Treatment	Group 1		Group 2		Group 3		χ^2 ^{c)}
	1st	2nd	1st	2nd	1st	2nd	
	TAP-031 200 μ g i.m. ^{a)}	TAP-031 500 μ g i.m.	TAP-031 500 μ g i.m.	TAP-031 500 μ g i.m.	HCG 10,000 MU i.m.	APG 400 KE i.v. ^{b)}	
No. of cows treated	53		58		49		
No. of cows inseminated after 1st treatment	22		17		21		
Average days to insemination	42 $\pm$ 22 ^{d)}		38 $\pm$ 24		38 $\pm$ 23		
No. of cows conceived within 90 days after 1st treatment	16		11		11		
Percent of cows conceived	30.2		19.0		22.4		1.98
Average interval in days between treatment and conception	48 $\pm$ 23		40 $\pm$ 27		45 $\pm$ 29		
No. of cows re-treated	26		36		25		
No. of cows conceived within 90 days after re-treatment	18		22		14		
Total No. of cows conceived	34		33		25		
Percent of total cows conceived	64.2		56.9		51.0		1.84
Average interval in days between initial treatment and conception	52 $\pm$ 23		54 $\pm$ 29		56 $\pm$ 24		

^{a)} Intramuscular injection. ^{b)} Intravenous injection. ^{c)} $\chi^2(2, 0.05)=5.99$. ^{d)} Mean $\pm$ S.D.

Table 2. Response of serum progesterone level in cows with cystic ovary 14 days after treatment with 200 or 500 μ g of an analog of LH-RH (TAP-031) and 10,000 MU of HCG

Treatment	No. of cows	Change in serum progesterone level			$\frac{a}{a+b} \times 100$ (%)	
		Increased (a)	Not changed (b)	Decreased (c)		
TAP-031 200 μ g i.m. ^{a)}	53	26	20	7	56.3	n.s. ^{b)}
TAP-031 500 μ g i.m.	58	28	25	5	52.8	
HCG 10,000 MU i.m.	49	26	23	0	53.1	

(a): Serum progesterone level increased by more than 1.0 ng/ml 14 days after treatment.

(b): Serum progesterone level did not fluctuate beyond 1.0 ng/ml 14 days after treatment.

(c): Serum progesterone level decreased by more than 1.0 ng/ml 14 days after treatment.

^{a)} Intramuscular injection.

^{b)} Not significant. $\chi^2=0.20$, $\chi^2(2, 0.05)=5.99$.

3,000 rpm for 10 minutes was stored at -20°C till analysis. Serum progesterone levels were estimated by enzyme immunoassay as reported elsewhere [8] to monitor the luteinization of follicular cysts.

The effect of treatment was first evaluated by conception within 90 days after treatment. It is summarized in Table 1. There was no significant difference in conception rate after the first treatment between the

three treated groups. The same trend was observed in conception rate following re-treatment and the interval of time between the initial treatment and conception.

Then an increase in serum progesterone level by 1.0 ng/ml or more 14 days after treatment was used as a criterion of positive response, i.e., the luteinization of follicular cysts. Of the 160 cows, twelve had pre-treatment serum progesterone levels

higher than 1.0 ng/ml and showed a decrease in these levels by more than 1.0 ng/ml 14 days after treatment. They were considered neither as positive nor as negative, because it was difficult to determine whether the decrease of serum progesterone level was induced by the effect of the treatment or not. It is also possible that the 12 cows may have had cystic or normal corpora lutea which sometimes could not be differentiated from follicular cysts by rectal palpation. Cows in which the serum progesterone level neither increased nor decreased by more than 1.0 ng/ml were judged as negatively responding ones. Therefore, the rate of positive cases was obtained from that of the number of positive cases to the total number of positive and negative cases. No significant difference was observed in it among the three treated groups, as shown in Table 2.

An i.m. injection with 10,000 MU of HCG has been a more popular method for the treatment of COD in cattle than any other hormone therapy in Japan. The present study revealed that there was no significant difference in therapeutic effect on COD between an i.m. injection with 200 or 500 μ g of TAP-031 and one with 10,000 MU or HCG.

An i.m. injection with 200 μ g of TAP-031 may be a choice for the treatment of COD in cattle, since an analog of TAP-031 can be synthesized. Therefore, such analog may be supplied at a reasonable price. It is not likely for antibody to be produced

by repeated injections with TAP-031, as is often seen after repeated administrations with HCG [7] because of the low molecular weight of TAP-031.

Acknowledgments. The authors thank the veterinarians of the Kuromatsunai, the Oshamambe, the Shimizu, the Memuro, the Sarabetsu, and the Nakasatsunai Veterinary Hospitals in Hokkaido who helped them in carrying out treatment trials. Their thanks are also due to Dr. Akira Kambegawa of the Teikoku Hormone Mfg., Co., Ltd., Tokyo, for his kind supply of antiserum to progesterone used for enzyme immunoassay. The supply of LH-RH analog (TAP-031) by the Takeda Chemical Industries Co., Ltd., Osaka, is acknowledged with thanks.

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要 約

乳牛卵胞嚢腫に対する黄体形成ホルモン放出ホルモン (LH-RH) 類縁化合物 (TAP-031) の治療効果 (短報): 中尾敏彦・河田啓一郎・沼田芳明 (酪農学園大学獣医学科)——乳牛卵胞嚢腫に対する黄体形成ホルモン放出ホルモン (LH-RH) 類縁化合物 (TAP-031) 200 μg と 500 μg および妊婦尿性腺刺激ホルモン (HCG) 10,000 MU の治療効果比較試験を行った. 初回治療後90日以内に受胎したものを有効例とした場合の有効率は, TAP-031, 200 μg 筋肉注射群で 30.2% (16/53), 500 μg 筋肉注射群で 19.0% (11/58), HCG 10,000 MU 筋肉注射群で 22.4% (11/49) であった. この成績から, TAP-031, 200 μg の投与により, 従来の HCG 10,000 MU とほぼ同等の治療効果が得られることがわかった.