EFFECT OF GONADOTROPHIN RELEASING HORMONE IN UNDERFED IMMATURE RATS

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Summary : An investigation on the effect of restricted feeding and GnRH treatment using immature rats of both sexes was made to see if the GnRH can produce its desired effect on the reproductive organs through the pituitary gonadal axis irrespective of the age and nutritional status of the animal. It was observed that immature male and female rats responded differently to the treatment of GnRH and responses are to a great extent age-dependent. Restricted feeding in these animals slowed down the growth of the reproductive organs.

Key words: restricted feeding GnRH pituitary gonads thymus

INTRODUCTION

Restricted calorie intake has been well established to adversely affect the reproductive functions in rats accompanied by decrease in weight of target organs (2,3,15). The effect of restricted feeding on hypothalamic LHRH content and pituitary function has been studied in relation to gonadal activities (5, 9, 10). The response of pituitary and gonads to GnRH administration was found to be age dependent (1, 4). It was also demonstrated that body weights, pituitary and ovarian weights were reduced in animals on restricted feed intake while the treatment with GnRH and glucose simultaneously resulted in body and organ weights similar to *ad lib* fed ones (6). It has also been shown that hypophyseal secretion of gonadotrophin in intact rats starts declining soon after the feed restriction is imposed (7). The effect of underfeeding on testosterone inhibited gonadotrophin secretion indicated that gonadotrophin level were higher in the underfed rats (8). It is now well established that hypothalamic peptidergic neurons produce releasing and inhibiting hormones that modulate the secretion of adenohypophyseal trophic hormones (6, 12, 13). Synthetic LRF has also been found to significantly decrease the weight of accessory sex organs

in immature male rats (11, 16). There is very little information in the literature as to the effect of GnRH treatment on underfed immature rats in relation to their pituitary and gonadal responsiveness The aim of the present study was to observe the response of hypothalamo-hypophyseal-gonadal axis of underfed prepuberal rats to GnRH administration about which no information is available.

MATERIALS AND METHODS

Twentyfive days old postweaned rats of IVRI strain of both sexes of similar weight were divided into eight groups. Four of these groups were kept under-nourished for seven days by giving daily half of the usual amount of ration whereas the other four groups were fed *ad lib.* All these animals were maintained in good sanitary condition at a comfortable temperature of 25 to 27°C with free access to water and in a lighting schedule of 14 light/24 hr. All the experimental animals were given an adequately balanced ration as per IVRI routine. The body weights of all the animals were recorded on alternate days. The body weights of underfed animals reduced by 20–25% compared to *ad lib* controls before they were given GnRH.

One group of each underfed and *ad libitum* rats of both sexes were given five daily injections of 0.2 *ml/day* (each *ml* of solution contained 0.004 *mg* of Buserelin) of synthetic GnRH. The corresponding controls were injected with 0.2 *ml/day* of physiological saline (9.00 *g/1*). After five injections the animals were sacrificed and the uteri, ovaries, testis, pituitary, epididymis, thymus and accessory sex organs from individual animals of control and treated groups were collected and weighed on a torsion balance having a sensitivity upto 0.2 *mg*.

The data was analysed statistically for test of significance by using student 't' test.

RESULTS AND DISCUSSION

Some workers have used indices like hypothalamic LRF content, level of receptors in target organs, pituitary gonadotrophin content and weights of pituitary and gonads to study the effect of underfeeding on the reproductive functions in both male and female animals. Normally underfeeding decreases the pituitary gonadotrophin levels and LHRH content of the hypothalamus (14), thereby indirectly reducing the ovarian and the uterine weights due to the absence of sufficient amount of oestrogens. In the present study (Fig. 1) in immature growing rats, similar results have been obtained. Both ovarian and uterine weights in underfed females were lower than those of the *ad lib* fed controls. Supplementing with GnRH did increase the uterine and ovarian weights of the underfed animals

whereas an opposite effect was observed in the *ad lib* fed treated rats. This showed that administration of GnRH to normal immature animals inhibited the pituitary function and indirectly thereby reduced ovarian function resulting in decreased uterine weights.

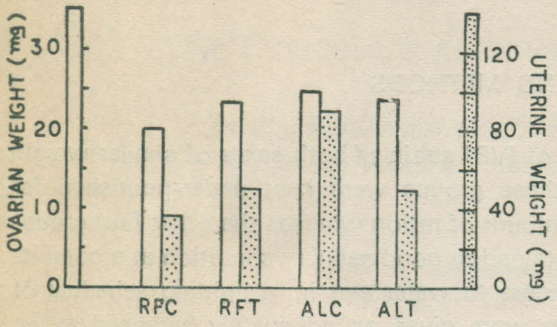

FIG. 1: THE OVARIAN AND UTERINE WEIGHTS.

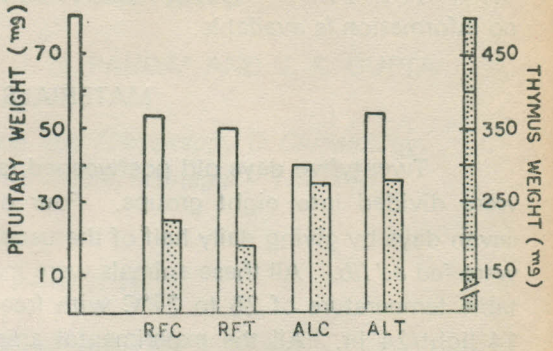

FIG. 2: THE PITUITARY & THYMUS WEIGHTS (FEMALE)

The pituitary weight has been shown to decrease in the female adult rats kept on restricted diet (6). The present findings show (Fig. 2) that the pituitary weight is higher in underfed animals than that of *ad lib* fed controls. When those animals were given GnRH, they failed to show any marked change whereas treatment with GnRH to *ad lib* fed rats caused increase in weight of the pituitaries. This indicated that GnRH can have stimulating effect on the pituitary of the immature females, if the nutritional requirements of the animal while growing are adequate. This may be perhaps due to the fact that synthetic activities of the pituitary under the stimulation of GnRH can only be possible when all the precursor amino acids and other energy supplying ingredients are available to the animal (7). The visible increase in pituitary weight (Fig. 2) in the restricted fed animals may be due to decreased synthesis and release of other hypothalamic hormones other than GnRH thereby causing on accumulation of hormones in the hypophysis.

The thymus weight decreased in underfed animals as compared to that of *ad lib* fed controls. Treatment with GnRH produced no significant effect in either underfed or *ad lib* fed animals over their respective controls (Fig. 2).

In the male rats restricted feeding significantly decreases the pituitary weight (8). The present study (Fig. 3) in growing immature underfed males, presented exactly a similar picture compared to their *ad lib* fed controls. When these animals were treated with GnRH, the pituitary weight increased in underfed animals with an opposite effect in *ad lib* fed ones as compared to the respective untreated controls. This is similar to earlier observations (16). Underfeeding caused a significant ($P<0.05$) fall in thymus weights (Fig. 4).

Testis weight were lower in underfed animals than that of *ad lib* fed ones. Injection of GnRH caused a significant ($P<0.01$) fall in the *ad lib* fed animals showing its antireproductive property, which is in agreement with earlier findings (16). Testicular weight of the underfed animals was not affected by GnRH. Epididymal weights (Fig. 3) were higher in restricted fed groups than *ad lib* fed ones.

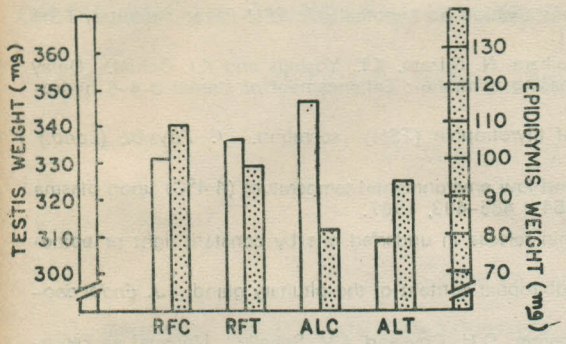

FIG. 3 : THE TESTIS AND EPIDIDYMAL WEIGHTS.

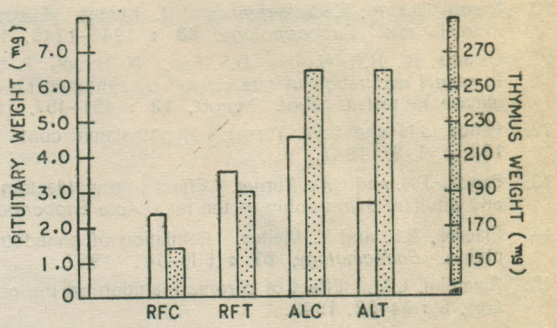

FIG. 4 : PITUITARY AND THYMUS WEIGHTS IN CONTROL AND TREATED GROUPS. (MALE)

In conclusion it can be said that, in the immature growing rats, restricted feeding slows down the development of the reproductive organs due to the decreased function of the hypothalamus and pituitary and even the gonads in both males and females. When these animals were treated with GnRH, both the sexes responded differently showing that the response or sensitivity of the pituitary to the hypothalamic releasing factors is controlled by different maturational changes in both the sexes which are possible age specific (1, 4).

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REFERENCES

1. Barnea, A. G. Cho and J.C. Porter. A role for the ovaries in maturational process of hypothalamic neurons containing LHRH. *Endocrinology*, **105** : 1303–1307, 1979.
2. Cooper, K.J. and N.B. Haynes. The effect of factors associated with the male on number of ovulations, uterine weight and pituitary LH content in the rat. *J. Reprod. Fert.*, **31** : 197–200 1972.
3. Cusan L., C. Auclair, A. Belanger, L. Ferland, P.A. Kelly, C. Seguin and F. Labrie. Inhibitory effect of long term treatment with LHRH agonist on the pituitary gonadal axis in male and female rate. *Endocrinlogy* **104** : 1369–1376, 1979.
4. Dhoble, R.L., S.K. Jindal J.N. Panda and S.K. Gupta. GnRH induced changes in reproductive organs of the rats. *Ind. J. Exptl. Biol.*, 1981.
5. Dickeoman E.A. A. Negro-Vilar and J. Meites. Effects of starvation on plasma GH activity pituitary GH and GH-RF levels in the rat. *Endocrinology*, **84** : 814–819, 1969.

6. Howland B.E. Effect of restricted feed intake on LH levels in female rats. *J. Anim. Sci.*, **34** : 445–447, 1972.
7. Howland B.E. Ovarian weight and ovarian compensatory Hypertrophy in the rat as affected by duration of underfeeding. *J. Reprod. Fert.*, **28** : 321–323, 1972.
8. Howland B.E. Effect of underfeeding on the inhibition of gonadotrophin secretion by testosterone propionate in rats. *J. Reprod. Fert.*, **55** : 335–338 1979.
9. Leathem, J.H. Hormones in growth and development : Hormones and protein nutrition. *Rec. Prog. in Hormone Research*, **14** : 141–176, 1958.
10. Negro-Vilar A., E. Dickerman and J. Meites. Effects of starvation on hypothalamic FSH-RF and pituitary FSH in male rats. *Endocrinology*, **88** : 1246–1249, 1971.
11. Oshima, H., H.R. Nankin D.F. Fan, P. Throen T. Yanaihara N. Niizato, K.I. Yoshids and K.I. Ochial. Delay in sexual maturation of rats caused by synthetic LH-releasing hormone : Enhancement of steroid d-4–5 hydrogenase in testes. *Biol. Reprod.*, **12** : 491–497, 1975.
12. Panda, J.N and C.W. Turner. Hypothalamic control of thyrotrophin (TSH) secretion. *J. Physiol.* (*Lond.*) **192** : 1–9, 1967.
13. Panda, J.N. and C.W. Turner. Effect of thyroidectomy and low environmental temperature (4·4°C) upon plasma and pituitary thyrotrophin in the rat. *Acta Endocrinol.*, **54** : 485–493, 1967.
14. Placsek, B.E. and T. Meites. Reiniation of gonadotrophin release in underfed rats by constant light or epinephrine. *Endocinology*, **81** : 535–541 1967.
15. Rinaldini, L.M. Effect of chronic inanition on the gonadotrophic content of the pituitary gland. *J. Endocrinology*, **6** : 54–62, 1949.
16. Tcholakian, R.K., A. dela Cruz M. Chowdury, A. Steinberger D.H. Coy and A.V. Schally. Unusual antireproductive properties of the analog LHRH thylamide in male rats. *Fertility and Sterility*, **30** : 600–603 1978.