EFFECT OF GONADOTROPHIN RELEASING HORMONE IN UNDERFED IMMATURE RATS


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(Received on February 9, 1981)

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 ones (6). It has also been shown that hypophyseal secretion of gonadotrophins 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, 12). The effect of GnRH treatment on responsiveness of the pituitary-gonadal axis in growing rats however, no information is available.

Twentyfive days old rats were divided into eight groups and seven days by giving daily injections of 0.2 ml/day (e GnRH. The correspondin pituitary, epididymis, thymus and treated groups were supplemented with GnRH did
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/l). 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 up to 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.

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 an 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).

**ACKNOWLEDGEMENTS**

The authors are thankful to Hoechst AG, Berlin for the continued supply of GnRH analogue used in this study.

**REFERENCES**


**SHORT COMMUNICATION**

**EVIDENCE FOR HISTAMINE LIKE EFFECTS OF MK-212 ON GUINEA PIG IILEUM**

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Summary: MK-212 (1x10^-6 M) ileum, taenia coli and rat fundus strip did not produce any significant effect upon ileum, taenia coli and rat fundus strip to MK-212. MK-212 did not produce any significant effect upon the ileum, taenia coli and rat fundus strip as well as histamine like effects.

Key words : MK-212 (6-Chloro-2-(1-piperazine), guinea pig ileum, guinea pig taenia coli, guinea pig fundus strip, guinea pig ileum, histamine.

6-Chloro-2-(1-piperazine) thylamide is a synthetic luteinizing hormone releasing hormone (LHRH) analog and is reported to produce sedation in the central nervous system. It causes increased strength of crossed extensor reflex, anorexigenic and ancillary effects upon the integrity of 5-HT nerves. It resembles fenfluramine, which...