

## CIRCADIAN RHYTHMICITY OF GROWTH HORMONE AT HIGH ALTITUDE IN MAN

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( Received on January 20, 1991 )

Circulatory levels of growth hormone (GH) were estimated at 0600 h, 1200 h, 1800 h and 2400 h in each of 10 subjects of sea level residents (SLR) in New Delhi (226 m) and in high altitude natives (HAN) settled at an altitude of 3650 m. Both in SLR and HAN the GH secretion showed an identical pattern, the values were lowest at 0600 h and highest at 2400 h. Nevertheless, in HAN the GH levels at different timings of the day were found to be significantly higher than in SLR.

**Key words :** high altitude                      growth hormone                      circadian rhythmicity

### INTRODUCTION

Observations on stress induced alterations in growth hormone (GH) secretion in man have revealed that all types of stress including surgery, electroshock therapy, physical exercise (1) and heat (2) are associated with elevation in GH levels. The hypoxic stress in man produces neuroendocrine responses of activation of the adrenocortical, adrenomedullary and sympathetic activity (3). These not only mobilise fuels to combat the stressful condition, but also appear to play an important role in the adaptation process. However, there is paucity of information on GH secretion during ascent to high altitude in man. In view of the observations that pituitary secretion of GH undergoes cyclic variations over the twenty four hour period (4) the hypoxic stress may be altering the GH rhythmicity. The plasma concentrations of growth hormone were therefore, measured at different timings of the day in a group of healthy sea level residents (SLR) and in high altitude natives (HAN).

### METHODS

Healthy euglycemic men, mean age 26.77 years (range 19-30 years) mean height 169.5 cm (range

157-178 cm), and mean body weight 59.8 kg (range 49.6-69.5 kg) formed the subjects of the study. The sea level studies were performed in September at New Delhi (226 m) when maximum atmospheric temperature range was 30-37°C and minimum 20-27°C. The high altitude studies were conducted on the highlanders settled in Western Himalayas, where maximum atmospheric temperature ranged from 16-20°C and the minimum from 4-8°C. The purpose and protocol of the study were explained to all the subjects and consent was obtained for their participation. The time sequence for circadian rhythm studies was 0600 h, 1200 h, 1800 h and 2400 h. These subjects received their usual meals consisting of breakfast at 0830 h, lunch at 1300 h, evening tea at 1700 h and dinner at 2000 h. The 0600 h samples were drawn after an overnight fast (10 h). All the subjects performed their routine duties and reported for the blood samples an hour earlier. For obtaining the 2400 h sample, they slept at 2200 h in the investigation room without any sedation. All of them were awake when the blood samples were collected. Samples were separated and plasma stored at -20°C until assayed for GH by radioimmunoassay (5). The anti-hGH rabbit serum and hGH reference standard (NIAMDD-hGH-RP-1) were obtained from NIAMDD, Bethesda, Maryland. The sensitivity

of GH assay was 0.25 ng/ml. The coefficient of variation of intra and interassay variations at different points was less than 10%. The statistical analyses were done using two way analysis of variance (Newman Keuls multiple range test). In case where the variance are not equal between SLR and HAN the comparison was made using Welsch procedure of modified student's test.

## RESULTS AND DISCUSSION

Both in SLR and HAN the GH levels were lowest at 0600 h and highest at 2400 h. In SLR, the GH levels at 1200 h and 1800 h were not significantly different from the 0600 h values but were significantly lower than the 2400 h values. In HAN, though the 1200 h and 1800 h values appear to be higher than the 0600 h, the change was not statistically significant. The 2400 h GH levels in HAN were significantly higher than the 0600 h, 1200 h and 1800 h values. In HAN, the GH levels at different timings of the day were significantly higher compared to the LSR values (Table I).

TABLE I : Mean  $\pm$  SE of growth hormone at different times of the day in sea level residents (SLR) and high altitude natives (HAN).

	Sea level residents (n=10)	High altitude natives (n=10)	P SLR Vs HAN
0600h	0.65 $\pm$ 0.15	4.10 $\pm$ 1.20	<0.05
1200 h	1.40 $\pm$ 0.46	7.98 $\pm$ 1.84	<0.01
1800 h	1.41 $\pm$ 0.23	12.21 $\pm$ 5.10	<0.05
2400 h	8.38 $\pm$ 3.00*	20.47 $\pm$ 4.82*	<0.05

\*P Vs 0600 h <0.01

The results of the present study demonstrate that the natives of high altitude have higher circulatory levels of GH, as compared to their counterparts

at sea level. This elevation in GH is evident at all periods of the day. Nevertheless, the circadian rhythmicity of GH is well maintained in HAN albeit at a higher level. The exact reason for this increase in GH remains unknown. An increased pituitary secretion of hormone, and or a delay in its clearance rate; or some combination of factors like oxygen deficit or muscle hypoxia (6) may be contributing factors. It does not appear that this elevation of GH in HAN was due to altered carbohydrate intake, or hypoxia induced decrease in blood glucose. The SLR consumed a diet of 3500 Kcals per day (proteins 14.6%, fats 24.9% and carbohydrates 60.5%) whereas the HAN consumed a diet of 4320 Kcals per day (proteins 11.90%, fats 26.3% and carbohydrates 61.8%). The consumption of carbohydrates in HAN was in fact higher, being 746 gms/day compared to 619 gms/day of SLR. The fasting (0600 h) glucose values in HAN were found to be higher than in SLR, though glucose pattern in HAN at different timings of the day was identical to that of SLR (7). The present observations of increase in GH at high altitude are in agreement with those of Raynaud et al (8). These indicate that GH secretion at high altitude is under normal physiological regulation which is further augmented by the sleep stimulus. The physiological significance of elevated GH at high altitude can only be surmised. It may have some somatotrophic role in maintaining organ hypertrophy of heart and lung (9) and other metabolic effects as part of adaptive phenomenon. Further studies are in progress to ascertain the role of growth hormone in metabolic adaptation to the hypoxic stress, especially the response of SLR at high altitude during the acclimatization period.

## ACKNOWLEDGEMENTS

The authors are grateful to Dr. B.N. Chaudhuri former Director of the Institute for criticism and suggestions and to Dr. D.P. Chattopadhyay for reviewing the manuscript. Technical assistance of Mr. Thakuri Singh, statistical assistance of Mr. A.K. Ghadiok and secretarial assistance of Shri Omparkash are also acknowledged.

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