Letters to the Editor

Basal and Stimulated Growth Hormone Levels in Children with Cirrhotic Disorders

Failure of linear growth or malnutrition complicates chronic liver disease in children in about 50% of cases. It is known that chronic liver disease is associated with development of growth hormone (GH) resistance, characterized by high circulating GH, low IGF-l concentration(1,2) and reduced GH receptors present on cirrhotic liver(3).Also there is discrepant literature available regarding response to standard GH replacement therapy in childhood liver disease.

We at our center evaluated the basal and stimulated GH levels in children with cirrhosis of liver. Fifteen prepubertal children diagnosed to have cirrhosis of liver and seven children (age range of 5-l1 years) with non-GH deficient short stature as controls, were studied. The clinical and biochemical characteristics of the two groups are given in *Table 1*. Liver functions were marginally elevated in study group and were grouped under Childs' class 'A' in terms of

TABLE I–*Mean±SD of Clinical and Biochemical Characteristics in Study and Control Group.*

	Study group (n = 15)	Control group (n = 7)
1. Chronological age in years	8.3 ± 2.3	8.3 ± 1.8
Male children	9.0 ± 1.3 (n = 10)	7.5 ± 1.9 (n = 4)
Female children	7.0 ± 3.3 (n = 5)	9.5 ± 1.3 (n = 3)
2. Bone age in years	8.0 ± 2.2	7.5 ± 1.7
Male children	8.7 ± 1.4	6.5 ± 1.2
Female children	6.6 ± 3.2	8.6 ± 0.5
3. Height in cm	109.7 ± 11.7	113.5 ± 9.5
Male children	112.5 ± 9.3	108.3 ± 8.8
Female children	104.1 ± 15.1	120.0 ± 5.5
No. of children >3 SD below mean height	11	7
4. Body weight (kg)	17.5 ± 4.1	18.2 ± 3.0
Male children	18.3 ± 3.0	17.2 ± 2.7
Female children	15.9 ± 5.7	19.6 ± 3.5
5. Percent ideal body weight of total	73.9 ± 5.9	79.0 ± 5
6. S albumin	3.5 ± 0.2	3.7 ± 3.3
7. SGOT	35.1 ± 16.4	17.1 ± 3.3
SGPT	39.1 ± 14.83	18.85 ± 3.5
8. GH profiles (ng/mL)		
Baseline	2.1 ± 1.1	2.4 ± 0.8
Clonidine stimulated*	6.32 ± 4.4	12.3 ± 4.4
Bromocriptin stimulated†	5.7 ± 4.7	10.6 ± 3.3

* P = 0.008, † P = 0.025.

hepatic-functional reserve. Control group had normal GH response to provocative stimuli (bromocriptin and clonidine), GH response was significantly lower in study group than in controls. Blunted GH response (rise in level of GH <10 ng/mL) was found in 80% of patients with bromocriptin and 60% of patients with clonidine and none in control group.

Impaired liver function is known to cause decrease in somatomedin secretion and in turn lead to higher GH secretion through negative feedback mechanism. Since these patients may also be nutritionally deficient, raised GH levels might be an attempt to improve the aminoacid utilization and protein synthesis, as observed in protein calorie malnutrition(4). But the blunted GH response to provocative stimuli observed in our patients may be due to dysregulation of hypothalamo-pituitary-IGF axis to provocative stimuli and also liver function derangement is not so severe to cause raised basal and stimulated GH levels. Finally there could be unidentified factors that affect the GH responsiveness to provocative stimuli acting through different regulatory pathways of GH secretion namely dopaminergic pathway, cholinergic pathway *etc*. So keeping aside, well known limitations of provocative GH testing, this blunted response of GH levels would have probably made more sense in light of serum IGF-1 estimation.

Since GH resistance in liver disorders is observed with progression of liver disease, therapeutic response to GH therapy would be confounded by GH resistance in them, and this may be relevant to use of GH therapy in cirrhotic children(5,6). Our observations make it imperative to consider dysregulation of GH secretion and not the GH insensitivity in children with cirrhosis of liver at least in early stage of the disease. The standard GH therapy might be beneficial in these children.

Biplab Bandhyopadhyay,
D.V.S. Reddy,
S.K. Singh*,
Department of Endocrinology and Metabolism,
Institute of Medical Sciences,
Banaras Hindu University,
Varanasi 221 005, India.
**Corresponding author*

REFERENCES

1. Donaghy A, Ross R, Gimson A, Hughes SC, Holly J, Williams R. Growth hormone, insulin-like growth factor-1, and insulin-like growth factor binding proteins 1 and 3 in chronic liver disease. Hepatology 1995; 21: 680-688.
2. Holt RIG, Jones JS, Stone NM, Baker AJ, Miell JP. Sequential changes in insulin like growth factor-1 (IGF-1) and IGF binding proteins in children with end stage liver disease before and after successful orthotopic liver transplantation. J Clin Endocrinol Metab 1996; 81: 160-168.
3. Shen XV, Holt RI, Miell JP, Justice S, Portmann B, Poztal-Vinay MC, *et al*. Cirrhotic liver expresses low levels of the full length and truncated growth hormone receptor. J Clin Endocrinol Metab 1998; 83: 2532-2538.
4. Raghuramulu N, Jaya Rao. Growth hor-mone secretion in protein calorie malnutrition. J C1in Endocrinol Metab 1974; 3: 176.
5. Cuneo RC, Hicman PE, Wallace JD, Teh BT, Ward E, Veldhuis JD, *et al*. Altered endogenous growth hormone secretory kinetic and diurnal GH binding protein profiles in adults with chronic liver disease. Clin Endocrinol Oxf 1995; 43: 265-275.
6. EI-Hawy-AM, Seif-el-Nasr-MS, Mahgoub-MA, Mostafa-N. Correlation between the level of serum growth hormone: somatomedin C; anthropometric measurement and the liver function in chronic liver diseases. J Egypt Soc Parasitol 1991; 21: 229-242.