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A STUDY OF SERUM PROLACTIN AND PLASMA HUMAN GROWTH HORMONE IN MALE ALCOHOLICS

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ABSTRACT

Serum levels of prolactin (PRL) and Human Growth Hormone (HGH) were assayed in 38 male alcoholics and 24 male control subjects using radioimmunoassay (RIA) technique. Biochemical parameters of hepatic function and severity of withdrawal state were also assessed. Significantly elevated values of plasma HGH were found in alcoholics as a group. Nineteen percent and eight percent of the patient had elevated serum PRL and HGH levels respectively. Evidence of advanced liver disease was scant and withdrawal symptoms were by and large mild. The findings indicate a dysfunction in hypothalamic adenohypophyseal axis in a subgroup of alcoholics.

Key Words : Prolactin, human growth hormone, alcoholics, alcohol withdrawal

Chronic alcohol consumption may alter prolactin (PRL) secretion in several ways. A transient rise in serum PRL level during withdrawal state (Wilkins et al., 1988; Miller et al., 1986; Castilla et al., 1987) has been described in chronic alcoholics. The rise may also occur with disappearance of withdrawal features indicating an inverse relation between serum PRL level and severity of withdrawal in alcoholics (Mazumdar, 1982; Samochowiec et al., 1995). Finally, while PRL secretion may be normal in alcoholics having intact hepatic function (Chiodera et al., 1981; Morgan, 1982), elevated values are reported in those with cirrhosis of liver (Noth & Walter, 1984).

Reports on the pattern of human growth hormone secretion (HGH) in chronic alcoholics seem to vary considerably across the studies. Basal plasma HGH levels are reported to be normal in chronic alcoholics who did not have any significant liver disease (Ganda et al., 1978) although higher values are reported in alcoholics with (Kuska et al., 1978; Yamaguchi et al., 1979) or without (Kuska et al., 1978) advanced liver disease. Challenge tests with insulin, propranolol and glucagon, however, are reported to evoke a blunted HGH response (Noth & Walter, 1984) probably indicating a reversible syndrome of HGH deficiency in a significant proportion of alcoholics (Wright, 1980).

These reports are mainly from the West. Data on Indian patients are non existent which could very well be different. This is evident through variable incidence of alcohol related liver damage in several countries (Mendenhall, 1993). In this study we attempted to explore i) the alterations in serum PRL and plasma HGH values among patients with alcoholism, ii) the reversibility of the hormonal changes, if any, from first to fourth week of abstinence and (iii) The severity of withdrawal symptoms and liver damage among the patients as the confounding factors affecting the hormonal changes. It has been suggested in the literature (Wright, 1980; Noth & Walter, 1984; Miller, 1986) that studies of endocrine changes including PRL & HGH may have implications in the pathophysiology as well as tissue damage related to alcoholism.

MATERIAL AND METHOD

The patients were adult males (N=38), (age 16-60 years) satisfying DSM - III (APA,1980) criteria of alcohol dependence. They were admitted for the treatment of alcoholism to the National Institute of Mental Health & Neurosciences (NIMHANS), Bangalore. The exclusion criteria were (i) presence of concurrent psychiatric disorder e.g., schizophrenia, major afective disorder as per DSM-III criteria, (ii)

dependence on other drugs of abuse, (iii) presence of diabetes mellitus and (iv) concomitant use of steroids, thyroid and antithyroid preparation.

The control group (N=24) consisted of physically healthy adult males (age 16-60 years). The exclusion criteria used for the patient group as mentioned above were also applicable to the control group. All the subjects included in the study gave their informed consent. The following were assessed within 48-72 hours of last alcohol intake.

1. A semistructured interview schedule was used to collect information on demographic and alcohol use data.
2. Clinical rating of alcohol withdrawal features were done by applying DSM-III (APA, 1980) criteria of alcohol withdrawal on a four point scale (0-3).
3. Venous blood sample was collected from the patients as well as control subjects between 8-9 AM in fasting state for hormonal and liver function test.

Blood samples were again collected after four weeks of stay in the hospital (2nd sample) for repeat investigation of hormone (s) and liver function. During this period the patients were strictly abstinent. The withdrawal sysmptoms were controlled by chlordiazepoxide 60-80 mg p.o. per day, and patients also received oral/parenteral vitamins. Liver biopsy (needle) was performed.

Hepatic function tests including serum bilirubin, total protein, albumin, aspartate amino transferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were analyzed by Hitachi 705 auto-analyzer.

Serum gammaglutamyl transpeptidase was assayed by the method described by Szass (1969). Hormone assays were carried out by radioimmunoassay (RIA) techniques, RIA kits from Leeco Diagnostics Incorporated, Michigan, USA (for PRL) and Bhaba Atomic Research Centre, Bombay, India (for HGH hormone) being used. Radiometric quantification was carried out by using compugamma, LKB, Wallac. The liver biopsy specimens were stained with haematoxylin, eosin, reticulin, PAS for glycogen and Masson's trichrome for the collagen.

Student's 't' test was used for statistical analysis. Modified 't' test (Rao et al., 1988) was employed where there was significant variance between two groups. This was done as an alternative to transformation of data to deal with the variance. Correlations were also attempted between the values of the hormonal levels and withdrawal rating score.

RESULTS.

The clinical data on the patients showed that their mean age was 35 years (34.5±7.7). Most of them started drinking around the age of 20 years (21.7±6.1). A great variability was seen in the duration (years) of dependence (2.7±3.7). The average daily consumption in the previous month was around 142 grams of ethanol (141.8±60.5).

The withdrawal severity rating score after 48-72 hours of the last drink was around 7 (7.7±1.9) which is about 35% of the maximum score of 20 possible on the scale. This indicated a mild degree of withdrawal and this was completely reversible by four weeks.

The laboratory parameters were interpreted against two frames of reference, viz. the laboratory reference values and the values of the control. The data of an individual patient was referred to the former whereas the latter was the reference for the entire sample.

TABLE 1

SERUM HORMONE LEVELS OF CONTROL GROUP AND PATIENTS (INTAKE)

Hormonal Parameters	Laboratory reference values (ng/ml)	Control (N=24)	Patients (N=38)	t	p
Prolactin (PRL)	0-15	12.25±4.99	17.64±31.64	0.97	NS*
Human growth hormone (HGH)	0-5	0.65±0.22	1.9±1.77	4.11	<0.001

*Modified 't' test was used.

The seurm PRL level was not significantly elevated in the alcoholics as a group. However, significant elevation of plasma HGH level was noted in alcoholics as a group ($p<0.001$) (Table-1)

Biochemical parameters indicating liver function & showed that values of serum AST (80.6± 85.4 Vs. 27.2±16.7) and GGT (139.8±142.7 Vs. 51.1±20.1) were significantly elevated in alcoholic patients during the first week. Other values of hepatic function including ALT were within normal laboratory range. There was marked variablility in the values of AST and GGT (Table-2).

Serum PRL and plasma HGH at fourth week (2nd sample) could not be assayed for ten patients as the sera was insufficient. However, for the remaining 28 patients the hormonal values at first week did not significantly differ from those at fourth week (Table-3). Significant improvement in hepatic function i.e. decline of the values of AST (81.8±35 Vs. 31.7±12.4), ALT (65.2±93.3 Vs. 29.3±16.3) and GGT (167.7 ± 163.6 Vs. 57.1±37 .1) was noticed after four weeks of abstinence (1st sample).

Furthermore, 19% and 8% of the alcoholics had elevated values of PRL and HGH respectively

TABLE 2

HEPATIC FUNCTION OF CONTROL GROUP AND PATIENTS (INTAKE)

Parametes of Liver function	Laboratory reference values	Control (N=24)	Patients (N=38)	p
Albumin	3.6-4.4 g%	4.5±0.5	4.2±0.4	<0.05
Total protein	6.8-8.6 g%	7.5±0.7	7.1±1.5	NS
Bilirubin	0.8-1 mg%	0.8±0.4	1.3±1.4	<0.05
Aspartate aminotramsferase (AST)	0-30 IU/L	27.2±16.7	80.6±85.4	<0.01*
Alanine aminotransferase (ALT)	0-30 IU/L	28.1±32.7	51±81.5	NS
Alkaline phosphatase (ALP)	35-110 IU/L	68.3±20.3	100.8±46.4	<0.05
Gamma glutamyl transpeptidase (GGT)	7-32 IU/L	51.1±20.1	139.8±142.7	<0.01*

* Modified 't' test was used.

TABLE 3

PLASMA HORMONE LEVELS OF THE PATIENTS (N=28) (FIRST AND FOURTH WEEK)

Hormonal Parameters	Laboratory reference values	Patients (first week)	Patients (fourth week)	t	p
PRL	0-15	11.86±8.98	19.73±21.56	1.53*	NS
HGH	0-5	1.95±1.81	1.69±1.57	0.80*	NS

* Modified 't' test was used.

(above laboratory normal range).

Liver biopsy findings were available only on eleven patients. The results showed that one person had a fatty liver, seven had alcoholic hepatitis and only one person had precirrhosis. None had classical findings of cirrhosis.

DISCUSSION

The subjects in this study were selected using DSM-III criteria and hence were relatively homogeneous on clinical vaiables. Blood (first) samples were collected 24 to 96 hours (mean2.7±1.9 days) after the last ethanol consumption so that the acute effects of ethanol on serum levels of PRL and HGH could be avoided.

We made three observations on the values of serum PRL in our patients. Firstly, the serum PRL levels in our alcoholics were normal. This was consistent with those reported by other authors (Chiodera et al., 1981; Morgan, 1982). Secondly, of the mean values of serum PRL at first and fourth week the latter was higher. This indicates a statistically nonsignificant trend in the rise of the serum PRL levels with the decline of the withdrawal features. Such a trend in PRL secretion in alcoholics was described in previous reports (Mazumdar, 1982; Samochowiec et al., 1995). Finally, 19% of the alcoholics had serum PRL value above the laboratory reference levels. Comparable figure (12%) was reported by Vanthiel et al. (1974). The significance of hyperprolactinaemia in subgroups of alcoholics is not clear. Clinically it may contribute to feminism (Valimaki & Ylikahri, 1985) whereas biochemically it may reflect a central hypodopaminergic state (Miller et al., 1986) in those patients.

The findings of significantly elevated basal plasma HGH level in our patients were consistent with a previous report (Kuska et al., 1978). Moreover, only 8% of the patients had raised levels (above laboratory normal range) of plasma HGH. The significance of higher plasma HGH values in alcoholics is not clear at present.

Alcoholic liver disease and severity of alcohol withdrawal may influence the hormonal secretion in alcoholics.

Alcoholic liver disease (mainly cirrhosis) has been cited as a strong contributory factor to altered secretion of PRL (Noth & Walter, 1984) and HGH (Kuska et al., 1978; Yamaguchi et al., 1979). However, evidence of advanced liver disease was scant in our sample. Biochemical parameters of hepatic dysfunction returned to normal by fourth week and the histology suggested a low incidence of cirrhosis as evidenced by the absence of classical cirrhotic changes in our sample of alcoholics.

The stress of withdrawal state also affects PRL and HGH secretion (Noth & Walter, 1984). A positive correlation between serum PRL levels and withdrawal rating score was reported in the previous studies (Wilkins et al., 1986; Castilla et al.; 1987). We found a rather weak positive correlation (r=0.2518) in our patients. The values of plasma HGH did not correlate (r=-0.0334) in any meaningful way. The lack of significant correlations between the hormonal values and severity of withdrawal could be due to the small sample size in our study. Moreover, only 19% and 8% of the patients had elevated levels of PRL & HGH respectively. Although plasma HGH values were significantly elevated among the alcoholics as a group serum PRL levels were not. It is possible that a mild degree of withdrawal state (mean 7.8 ± 1.9, maximum possible score 20) in our alcoholics did not strongly contribute to the hormonal changes.

Reversibility of serum hormonal levels following abstinence could not be demonstrated and reversibility of liver function tests seen in this study were in keeping with earlier reports (Eckhardt et al., 1984).

We conclude that altered PRL and HGH secretion may occur in a subgroup of patients with alcoholism. These changes are likely to be independent of liver disease as majority of our patients did not have evidence of advanced liver disease. These alterations may indicate dysfunction of hypothalamic-adenohypophyseal axis related to alcohol withdrawal state. Future studies using hypothalamic releasing factors may further resolve the issue.

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