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

SOMNATH SENGUPTA, RAJAT RAY, NIMESH DESAI & K. TARANATH SHETTY

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 adenohypophysial 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 affective disorder as per DSM-III criteria, (ii)
dependence on other drugs of abuse, (iii) presence
of diabetes mellitus and (iv) concomitant use of ste­
roids, thyroid and antithyroid preparation.

The control group (N=24) consisted of physi­
cally healthy adult males (age 16-60 years). The ex­
clusion criteria used for the patient group as men­
tioned 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 fea­
tures 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 be­
tween 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. Dur­
ing this period the patients were strictly abstinent.
The withdrawal symptoms 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 biliru­
binn, total protein, albumin, aspartate amino trans­
ferase (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 radioimmunoas­
say (RIA) techniques, RIA kits from Leeco Diagnos­
tics Incorporated, Michigan, USA (for PRL) and
Bhaba Atomic Research Centre, Bombay, India (for
HGH hormone) being used. Radiometric quantifica­
tion 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 analy­
sis. Modified 't' test (Rao et al., 1988) was employed
where there was significant variance between two
groups. This was done as an alternative to transfor­
mation of data to deal with the variance. Correlations
were also attempted between the values of the hor­
monal 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 dura­
tion (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.

| 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 horm­
none (HGH)          | 0-5                               | 0.65±0.22     | 1.9±1.77       | 4.11 | <0.001 |

Modified 't' test was used.
PROLACTIN AND HUMAN GROWTH HORMONE IN ALCOHOLISM

The serum 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 variability 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)

| Parameters 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                   | 0.8-1.0 mg%                 | 0.8±0.4       | 1.3±1.4        | <0.05|
| Aspartate aminotransferase (AST) | 0-30 IU/L          | 27.2±16.7     | 80.6±38.5      | <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.
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 variables. Blood (first) samples were collected 24 to 96 hours (mean 2.7 ± 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; Samochowicz et al., 1995). Finally, 19% of the alcoholics had serum PRL value above the laboratory reference levels. Comparable figure (12%) was reported by Vauthiel et al. (1974). The significance of hyperprolactinaemia in subgroups of alcoholics is not clear. Clinically it may contribute to feminism (Valininki & 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-c-adrenohypophysal axis related to alcohol withdrawal state. Future studies using hypothalamic releasing factors may further resolve the issue.

**REFERENCES**

American Psychiatric Association (1980) Diagnostic and Statistical Manual of Mental Disorders. 3rd edition (DSM-III). Washington DC, Ameri-
PROLACTIN AND HUMAN GROWTH HORMONE IN ALCOHOLISM

Castilla Garcia, A.; Santoloria Fernandez, F. J.; Gonzalez Reimers, C. E.; Batista Lopez, N.; Gonzalez Garcia, C.; Jorge Hernandez, J. A. & Hernandez Neito, L. (1970) Alcohol induced hypogonadism: Reversal after hormonal withdrawal. Drug and Alcohol Dependence, 20(3), 255-260.

Chiodera, P.; Pignatli, D.; Maestri, E.; Zanardi G.; Degliantoni, G.; Orlando, S.; Volpi, R. & Delsignore, R. (1981) Blood level of prolactin, dehydroepiandrosterone sulfate, cortisol, testosterone, 17-B estradiol in chronic alcoholism. Gioranale di Clinica Medica, 62(7), 437-442.

Eckhardt, M. J.; Rawlings, R. R.; Ryback, R. S.; Martin, P.R. & Gottschalk, L.A. (1984) Effects of abstinence on ability of clinical laboratory tests to identify male alcoholics. American Journal of Clinical Pathology, 82, 305-310.

Ganda, O.P.; Swain C. T. & Iber, F. (1978) Transient suppression of growth hormone secretion after chronic ethanol intake. Alcoholism Clinical and Experimental Research, 2, 297-299.

Kuska, J.; Krol, Z. & Libera, T. (1978) Studies on the mechanism of stimulation of growth hormone (IR-HGH) by glucagon in patients with chronic liver disease. Materia Medica of Poland, 10(1), 3-8.

Mazumdar, S. K. (1982) Serum prolactin concentration during the hangover phase of ethanol withdrawal syndrome. Neuroendocrinology letters, 4(4), 253-259.

Mendenhall, C. L. (1993) Alcoholic hepatitis. In: Diseases of the liver, vol 2, (Eds.) L. Schiff, E. R. Schiff. PP 856-874. Philadelphia : J. B. Lippincott Co.

Miller, F.; Barasch, A.; Sacks, M.; Levan, J. & Ashcroft, L. (1986) Serum prolactin correlates with depressed mood during alcohol withdrawal. Drug and Alcohol Dependence, 17(4). 331-338.

Morgan, M. Y. (1982) Sex and alcohol. British Medical Bulletin, 38, 43-48.

Noth, R. H. & Walter, R. M. (1984) The effect of alcohol on endocrine system. Medical Clinics of North America, 68, 133-146.

Rao, K.V.; Radhiaah, G. & Narayana, V. (1988) Statistics in Health and Nutrition. Proceedings of the national seminar, October 27-29, National Institute of Nutrition, ICMR, Jamai-Osmania, Hyderabad.

Samochowiec, J. & Horodnicki, J. (1995) A new view of the evaluation of alcohol withdrawal and alcohol dependence. Psychiatry of Poland, 29(1), 139-149.

Szasz, G. (1969) Method of gammaglutamyl transpeptidase assay in serum. Clinical Chemistry, 50, 124-126.

Valimaki, M. & Ylikahri, R. H. (1985) Endocrine effects of alcohol. In : Progress in alcohol research, vol.1, (Eds.) Parvez, S.; Burov, Y.; Parvez, H.; Burns, E., PP 265-286, Netherlands.

Vanthiel, D. H.; Lester, R. & Sherivs, R. H. (1974) Hypogonadism in alcoholic liver disease, Evidence for a double defect. Gastroenterology, 67, 1188-1199.

Wilkins, J. N. & Gorelick, D. A. (1986) Clinical neuroendocrinology and neuropharmacology of alcohol withdrawal. In : Recent Developments in Alcoholism, Vol.4, (Ed.) Galanter, M. PP 241-263. New York : Plenum Press.

Wright, J. (1980) Endocrine disease in the alcoholics. Medical consequences of alcohol abuse, 282, 157-170. Chichester : Ellis Horwood Limited.

Yamaguchi, K.; Fukushima, H & Uzawa, H. (1979) Response of human growth hormone, prolactin and thyrotropin to thyrotropin-releasing hormone in liver cirrhosis and diabetes mellitus. Endocrinology of Japan, 26 (1), 81-88.

Somnath Sengupta*, M.D., Associate Professor, Department of Psychiatry, Kasturba Medical College, Manipal, 576 116, Karnataka.

Rajat Ray, M.D., Nimesh G. Desai, M.D., Additional Professor, Department of Psychiatry, AIIMS, New Delhi - 110 029.

K. Taranath Shetty, M. Sc., Ph. D., Additional Professor, Department of Neurochemistry, NMHANS, Bangalore 560 029.

*Correspondence