Eur Arch Psychiatr Neurol Sci (1988) 237:317–319

European Archives of Psychiatry and Neurological Sciences

Guillain-Barré Syndrome and Serum Activities of Gamma-Glutamyltransferase and Glutamic-Pyruvic Transaminase

J. Kornhuber, A. W. Kornhuber, Ch. H. Kaiserauer, and W. E. Wanner

Department of Neurology, University of Ulm, D-7900 Ulm, Federal Republic of Germany

Summary. Objective laboratory indicators of alcohol consumption (mean corpuscular volume and serum glutamic-pyruvic transaminase (GPT), glutamyltransferase (γ-GT), and glutamic-oxaloacetic transaminase (GOT)) were measured in 18 patients with Guillain-Barré syndrome (GBS) and 710 control patients. All of the indicators examined were more frequently found to be pathological in GBS patients, reaching significance for γ-GT and GPT. Some explanations for this result are discussed. It is concluded that alcohol consumption may be a risk factor for GBS.

Key words: Guillain-Barré syndrome – Risk factors – Alcohol consumption – Blood-brain barrier – Blood-nerve barrier – γ-GT – GPT – GOT

Introduction

Guillain-Barré syndrome (GBS) is an acute inflammatory demyelinating disease of the nerve roots and peripheral nerves [1]. A partly virally induced, autoimmune process is thought to be the major factor in the pathogenesis of this disease [1]. Interestingly, in experimental allergic neuritis (EAN), the best experimental model for GBS, a disturbance of the blood-nerve barrier occurs during the earliest stages of the disease [5, 12]. The increase in vascular permeability is reported to either coincide with [5] or precede [12] the early histological indicators. These indicators include the appearence of perivascular and diffuse endoneurial edema and the migration of inflammatory cells into the endoneurial interstitium. These early events in EAN are suggestive of an important role for blood-nerve barrier disturbances in the initial stages of immune-mediated demyelination.

We have recently demonstrated that alcohol consumption causes a dose-dependent increase in the permeability of the human blood-brain barrier [8]. This stimulated consideration of the idea that toxic, infectious, or even autoaggressive substances could have increased access to the nervous system following increased alcohol consumption. Despite some known differences between the blood-brain and blood-nerve interfaces [9], these two barriers share many properties. Therefore, it is hypothesized that changes in the blood-nerve barrier also occur with excessive alcohol consumption. The present investigation was carried out to examine whether alcohol consumption is a risk factor for GBS.

Patients and Methods

The test group consisted of 18 patients, admitted to hospital between 1984 and 1986, fulfilling the NINCDS criteria for the diagnosis of GBS [2]. All of these patients underwent lumbar puncture; in most cases the typical enhancement in CSF total protein and normal cell count were observed. The control group consisted of all other patients (age- and sex-matched) treated in the hospital at the same time who also underwent a spinal tap ($n = 710$). Both GBS patients and controls came from the same area in Southern Germany.

Erythrocyte mean corpuscular volume (MCV), γ-glutamyltransferase (γ-GT), serum glutamic-oxaloacetic transaminase (GOT), and serum glutamic-pyruvic transaminase (GPT) were

Offprint requests to: J. Kornhuber's present address: Nervenklinik der Universität Würzburg, Füchsleinstrasse 15, D-8700 Würzburg, Federal Republic of Germany

Table 1. Case data and percentage of pathologic indirect indicators of alcohol consumption in Guillain-Barré syndrome and control patients

	Guillain-Barré syndrome	Controls
n (male/female)	18 (15/3)	710 (598/112)
Age (years)	39 (18–70)	41 (16–82)
γ-Glutamyltransferase	44.4%*	22.3%
Glutamic-pyruvic transaminase	38.9%*	20.0%
Glutamic-oxaloacetic transaminase	16.7%	12.5%
Mean corpuscular volume	16.7%	12.0%

*$P<0.05$

measured as objective, albeit indirect, indications of alcohol consumption. All parameters were determined by routine medical laboratory analysis. Blood samples were taken on admission to hospital. Differences in γ-GT, GOT, and GPT activities have previously been found between males and females. Therefore, mean values were not studied, but rather the percentage with elevated enzyme activities, using different limits for the normal ranges for men and women. The following values were regarded as normal: MCV < 98 fl for men and women; for men: γ-GT < 28 units/l, GPT < 22 units/l, GOT < 18 units/l; for women: γ-GT < 22 units/l, GPT < 20 units/l, GOT < 16 units/l. In the GBS patients, there was no evidence for prior drug treatment that might possibly have effected the parameters measured. The two-tailed χ^2 and Wilcoxon tests were used for statistical analysis; *P* values greater than 0.05 were regarded as not significant.

Results

All parameters measured indicative of enhanced alcohol consumption were more frequently pathological in GBS patients, reaching significance for γ-GT and GPT (Table 1). The mean values for γ-GT and GPT were clearly, but not significantly, enhanced in GBS patients (males and females together, GBS patients 45 units/l and 32 units/l respectively versus controls 22 units/l and 17 units/l respectively).

Discussion

There are several possible explanations for the observed enhancement in GBS patients of known indirect indicators for alcohol consumption. First, a change in liver function might be due to the disease process itself rather than due to alcohol consumption. Second, the suppression of the immune system occurring during excessive alcohol consumption [11] might produce increased susceptibility to infections which are thought to play a causative role in GBS. Third, the disturbance of the blood-brain [8], and presumably also blood-nerve barriers, seen with excessive alcohol consumption might constitute a risk for GBS.

Several findings, all of which emphasize the importance of disturbed blood-nerve barrier in the pathogenesis of GBS, fit with the third hypothesis. (1) As mentioned previously, blood-nerve barrier changes occur during the earliest stages of EAN [5, 12]. Conceivably, once the lesions have begun in EAN animals additional damage may be produced by serum-mediated factors that pass into the nerve at the site of abnormal vascular permeability. (2) Serum from both GBS patients [13] and from rabbits with EAN [6, 14] is capable of producing demyelination when injected directly into a peripheral nerve in rats, but not when injected systemically [7]. This difference might be attributable to the blood-nerve barrier which, under normal circumstances, prevents access of humoral factors to the endoneurial space. (3) In most cases pathological changes in EAN [5] and GBS start at the nerve roots and spread from there to the peripheral nerve. This means that the disease starts in a region where the blood-nerve barrier of a normal animal has a high permeability [10]. (4) The viability of the blood-brain barrier, and probably also the blood-nerve barrier, depend on sex and age, being more permeable in older patients and males [8]. Similarly, the frequency of GBS is greater in older patients and males [3, 15]. (5) The incidence rate for GBS has increased over the last few decades in the United States [3]. This might be due to enhanced alcohol consumption over this period.

Our unselected control group included some patients with diagnoses possibly related to alcohol abuse [4]. This was supported by the high incidence of pathological indicators of alcohol consumption in the control patients (Table 1). For this reason the difference between GBS patients and controls presented here is probably underestimated. The present case-control study showed that abnormalities in liver function tests exist in a considerable portion of patients with GBS. We suggest that alcohol consumption may be a risk factor for GBS. This, of course, is only a hypothesis which may be tested in further investigations. Although laboratory tests have more objectivity for diagnosis than self reports of alcohol consumption, which may be subject to denial, such tests are only moderately sensitive for detection of alcohol abuse. Therefore, a second study on the role of alcohol in the pathogenesis of GBS is required in which the prior alcohol intake of the patients can be more reliably controlled or evaluated.

Acknowledgement. We would like to thank Dr. R. Erickson for reading the manuscript. J.K. is recipient of a DFG scholarship.

References

1. Arnason BGW (1984) Acute inflammatory demyelinating polyradiculoneuropathies. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R (eds) Peripheral neuropathy, vol 2. Saunders, Philadelphia, pp 2050–2100
2. Asbury AK (1981) Diagnostic considerations in Guillain-Barré syndrome. Ann Neurol [Suppl] 9:1–5
3. Beghi E, Kurland LT, Mulder DW, Wiederholt WC (1985) Guillain-Barré syndrome. Clinicoepidemiologic features and effect of influenza vaccine. Arch Neurol 42:1053–1057
4. Gorman DM, Potamianos G, Williams KA, Frank AO, Duffy SW, Peters TJ (1987) Relationship between alcohol abuse and low back pain. Alcohol Alcoholism 22:61–63
5. Hahn AF, Feasby TE, Gilbert JJ (1985) Blood-nerve barrier studies in experimental allergic neuritis. Acta Neuropathol 68:101–109
6. Hahn AF, Gilbert JJ, Feasby TE (1980) Passive transfer of demyelination by experimental allergic neuritis serum. Acta Neuropathol 49:169–176
7. Hughes RAC, Kadlubowski M, Gray IA, Leibowitz S (1981) Immune responses in experimental allergic neuritis. J Neurol Neurosurg Psychiatry 44:565–569
8. Kornhuber J, Kaiserauer CH, Kornhuber AW, Kornhuber ME (1987) Alcohol consumption and blood-cerebrospinal fluid barrier dysfunction in man. Neurosci Lett 79:218–222
9. Low PA (1984) Endoneurial fluid pressure and microenvironment of nerve. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R (eds) Peripheral neuropathy, vol 1. Saunders, Philadelphia, pp 599–617
10. Olsson Y (1984) Vascular permeability in the peripheral nervous system. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R (eds) Peripheral neuropathy, vol 1. Saunders, Philadelphia, pp 579–597
11. Pitts TO, Van Thiel DH (1986) Urinary tract infection and renal papillary necrosis in alcoholism. In: Galanter M (ed) Recent developments in alcoholism, vol 4. Plenum, New York, pp 341–355
12. Powell HC, Braheny SL, Myers RR, Rodriguez M, Lampert PW (1983) Early changes in experimental allergic neuritis. Lab Invest 48:332–338
13. Saida T, Saida K, Lisak RP, Brown MJ, Silberberg DH, Asbury AK (1982) In vivo demyelinating activity of sera from patients with Guillain-Barré syndrome. Ann Neurol 11:69–75
14. Saida T, Saida K, Silberberg DH, Brown MJ (1978) Transfer of demyelination by intraneural injection of experimental allergic neuritis serum. Nature 272:639–641
15. Schonberger LB, Hurwitz ES, Katona P, Holman RC, Bregman DJ (1981) Guillain-Barré syndrome: Its epidemiology and associations with influenza vaccination. Ann Neurol [Suppl] 9:31–38

Received February 22, 1988