Eur Arch Psychiatry Clin Neurosci (1991) 241:69–72

European Archives of Psychiatry and Clinical Neuroscience

Original Articles

Liquorpheresis Eliminates Blocking Factors from Cerebrospinal Fluid in Polyradiculoneuritis (Guillain-Barré Syndrome)*

P.-J. Hülser[1], H. Wiethölter[3], and K. H. Wollinsky[2]

Departments of [1]Neurology and [2]Anaesthesiology/Intensive Care Medicine, Rehabilitation Hospital Ulm, Ulm University Academic Hospital, Oberer Eselsberg 45, W-7900 Ulm, Federal Republic of Germany
[3]Department of Neurology, University Hospital, Hoppe-Seyler-Str. 3, W-7400 Tübingen, Federal Republic of Germany

Received June 18, 1990

Summary. Cerebrospinal fluid (CSF) derived from six patients with polyradiculoneuritis (Guillain-Barré syndrome, GBS) treated by liquorpheresis was injected into rat sciatic nerve. By measuring spinal evoked potentials after stimulation of the tibial nerve, we observed slowing or dispersion of nerve conduction in those cases where the CSF had been taken before liquorpheresis. CSF of the same patient, sampled after liquorpheresis, showed minor effects only. Impairment of nerve conduction was seen between 5 and 20 min after injection, normal function being restored on the third day. These results suggest that liquorpheresis eliminates blocking factors from the CSF of patients with GBS. We postulate this as the effect by which liquorpheresis improves neurological symptoms in Guillain-Barré syndrome.

Key words: Polyradiculoneuritis – Guillain-Barré syndrome – Liquorpheresis – Injection of rat nerve – Impairment of conduction

Introduction

Polyradiculoneuritis (Guillain-Barré syndrome, GBS) and its animal model, experimental allergic neuritis (EAN), are considered autoimmune disorders of the peripheral neuron. Injection into rat nerve of serum derived from GBS patients [1, 2, 6, 8] or EAN animals [5] produces a conduction block. The factors responsible for this phenomenon are not known; immunoglobulins [8] and proteases [7] have been suggested. Clinically, we had observed a significant improvement in the neurological status of GBS patients after liquorpheresis [10, Wollinsky et al., this issue]. We therefore tested the blocking properties in rats of cerebrospinal fluid (CSF) of these patients collected before and after liquorpheresis in an experimental setting.

* Parts of this paper were presented at the symposion of the German Neurological Society, Bad Nauheim, 1989

Patients and Methods

CSF was taken from four patients with acute and two patients with chronic polyradiculoneuritis (GBS) before and after liquorpheresis with special filters (Pall Biomedicine Dreieich). Adsorption liquor-

Table 1.

Patient	Form	Number of LPH	Protein concentration before LPH	Protein concentration after LPH
M.B.	AIDP	1st	346	205
H.G.	AIDP	2nd	1100	488
H.E.	AIDP	2nd	320	257
K.K.	AIDP	8th	660	376
M.J.	CIDP	1st	514	249
R.M.	CIDP	6th	1476	768

AIDP = acute inflammatory demyelinating polyneuritis; CIDP = chronic inflammatory demyelinating polyneuritis; LPH = Liquorpheresis; protein concentration is given in [mg/l]

Table 2.

Patient	CSF	Latency of the spinal EP			Differences	
		prae Inj t_0 [ms]	5′ post Inj t_5 [ms]	20′ post Inj t_{20} [ms]	t_5-t_0 [ms]	$t_{20}-t_0$ [ms]
M.B.	prae LPH	2.6	2.6	3.0	0	0.4
	post LPH	2.7	2.7	2.8	0	0.1
H.G.	prae LPH	2.6	2.8	3.2	0.2	0.6
	post LPH	2.7	2.7	3.0	0	0.3
H.E.	prae LPH	2.5	2.6	2.8	0.1	0.3
	post LPH	2.8	2.9	3.0	0.1	0.2
K.K.	prae LPH	2.7	3.6	2.9	0.9	0.2
	post LPH	2.9	2.8	2.9	−0.1	0
M.J.	prae LPH	2.7	3.1	2.8	0.4	0.1
	post LPH	3.0	3.0	3.0	0	0
R.M.	prae LPH	2.6	2.9	3.0	0.3	0.4
	post LPH	2.7	2.8	2.8	0.1	0.1

EP = evoked potential; Inj = Injection; LPH = Liquorpheresis

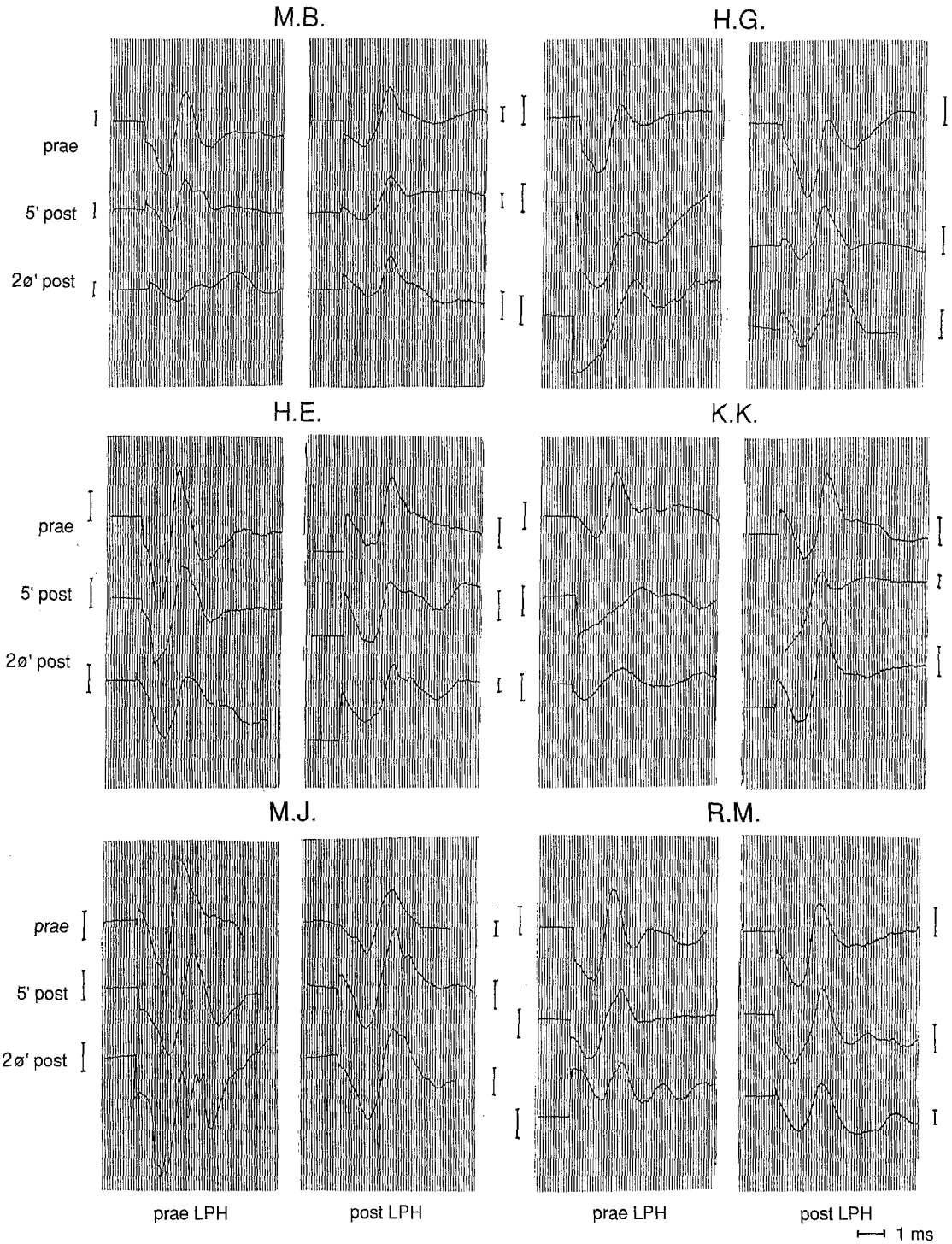

Fig. 1. Original recording of spinal evoked potentials (EP) after stimulation of the tibial nerve in rat. The right sciatic nerve was injected with CSF taken prior to liquorpheresis (prae LPH), the left with CSF of the same patient taken after liquorpheresis (post LPH). EPs were recorded before, 5 and 20 min after injection (prae, 5′ post, 20′ post, resp.). The *vertical bar* = 1 μV

pheresis decreased the protein content by about 50% (Table 1). CSF was stored at −80° until injection. We studied six female Lewis rats, weighing about 200 g, one animal for testing the CSF of each patient. After intraperitoneal anaesthesia with 5,6 dihydro-2-[2,6-xylidino]-4H-1,3-thiazinehydrochloride (Rompun, Bayer) and ketamine (Ketavet, Parke-Davis), 4.1 mg/kg and 47 mg/kg, the sciatic nerve was surgically exposed bilaterally. About 5 mm distal to the sciatic notch, 50 μl of CSF were carefully injected over one minute under the perineurium of the sciatic nerve via a 26-gauge needle. In each animal, CSF taken before liquorpheresis was applied to the right sciatic nerve, while CSF taken after liquorpheresis of the same patient was injected on the left side. The wound was closed suturing muscle and skin separately. After blocking of the sural nerve with 2% lidocaine, the tibial nerve was stimulated at the ankle joint using square-wave impulses of 0.2 ms duration at a frequency of 5 Hz, with intensity just above the motor threshold. The surface temperature of the animals was kept at 34°C by a sensor driven infra-red heater. The spinal evoked potentials were recorded between the spinal processes L_1/L_2 by a fine subcutaneously placed platinum electrode with a reference elec-

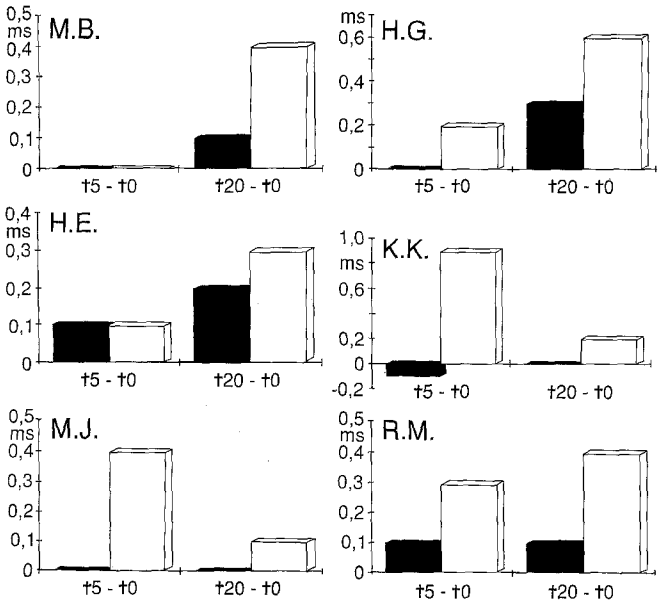

Fig. 2. Differences of latencies between recordings prior to (t_0) injection of CSF and after 5 min (t_5) and 20 min (t_{20}), were calculated (t_5-t_0, t_{20}-t_0). The *ligt columns* depict the results obtained with CSF taken prior to LPH, the *dense columns* the results with CSF taken after LPH

trode situated at the contralateral iliac crest. At a band pass filter of 10–1000 Hz we averaged 32–64 responses. This measurement was done before, 5 min, and 20 min after the injection of the sciatic nerve, as well as 3 and 7 days later.

Results

Injection of CSF taken before liquorpheresis caused an increase in latency of the spinal evoked potential. In two cases, the maximum delay was measured after 5 min, and in four animals after 20 min (Table 2, Fig. 1). On three occasions a dispersion of the impulse volley could be detected. Injection of CSF taken after liquorpheresis, however, regularly produced minor or no change of this response (Fig. 1). The differences between the latency of the spinal evoked potential before, 5 and 20 min after injection of sciatic nerve are shown in Fig. 2. In each case, their extent is greater when the nerve had been exposed to CSF taken prior to liquorpheresis. On days 3 and 7, the latencies after stimulation of the tibial nerve on the right and left sides did not differ.

Discussion

The recording of lumbar spinal evoked potentials provides a rapid and reproducible measurement of the conduction times of the proximal part of peripheral neurons, which are otherwise barely accessible [3]. This method has been successfully used to monitor the course of EAN [9]. The neurological status of six patients with GBS improved upon liquorpheresis [Wollinsky et al., this issue]. Assuming that this phenomenon was in fact caused by our novel therapeutic regimen we were interested in the physiological changes brought about by liquorpheresis. The injection of CSF from GBS patients under the perineurium of rat sciatic nerves was followed by a slowing of conduction or an increase of dispersion. Altered conduction properties could not be demonstrated to the same extent when CSF was taken after liquorpheresis. This fast and transient effect excludes demyelination or axonal damage. The observed alteration is compatible with a partial block of conduction.

Injection of serum derived from GBS patients [1, 2, 6, 8] or EAN animals [5] produces demyelination, to a lesser degree serum from healthy individuals [1, 6]. The relatively small effect observed in our experiments may be due to the low protein concentration of CSF compared with serum. Slowing of conduction, however, was obtained independent of the total protein content of our CSF probes. This implies a specific effect of unidentified factors in contrast to the assumption of unspecific action of proteins. All CSF samples were taken during the progressive phase of GBS; but, judging from this small number of tests, slowing or dispersion of conduction occurred with CSF obtained both in very early stages or in advanced disease, whether taken before the first or prior to any subsequent liquorpheresis. Serum from animals with experimental allergic encephalomyelitis produces demyelination in peripheral nerve and in spinal cord after injection into the subarachnoideal space [4]. This can be considered as evidence for the existence of a pathological factor common to demyelinating diseases. Further experiments are underway to clarify the reasons for the disturbed function of the myelin sheaths.

Removing pathological blocking factors from the immediate surrounding of spinal roots in polyneuroradiculitis Guillain-Barré led to clinical improvement. Adding complete CSF from GBS patients to surgically exposed rat sciatic nerves promptly provoked conduction impairment. Filtered CSF had no or minor blocking effect. We hypothesise that removal of blocking factors is responsible for the therapeutic efficacy of liquorpheresis in Guillain-Barré syndrome.

References

1. Feasby TE, Hahn AF, Gilbert JJ (1982) Passive transfer studies in Guillain-Barré polyneuropathy. Neurology 32: 1159–1167
2. Harrison BM, Hansen LA, Pollard JD, McLeod JG (1984) Demyelination induced by serum from patients with Guillain-Barré syndrome. Ann Neurol 15:163–170
3. Hülser P-J, Wiethölter H (1986) The anterior root response in the lumbar SEP of rat after stimulation of the tibial nerve. Electromyogr Clin Neurophysiol 26:49–55
4. Lassmann H, Kitz K, Wisniewski HM (1981) In vivo effect of sera from animals with chronic relapsing experimental allergic encephalomyelitis on central and peripheral myelin. Acta Neuropathol (Berl) 55:297–306
5. Saida K, Saida T, Brown MJ, Silberberg DH, Asbury AK (1978) Antiserum mediated demyelination in vivo – a sequential study using intraneural injection of experimental allergic neuritis serum. Lab Invest 39:449–462
6. 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

7. Schabet M, Schott K, Stevens A, Wiethölter H (1989) Therapie der experimentellen allergischen Neuritis (EAN) mit Protease-Inhibitoren. In Fischer PA, Baas H, Enzensberger W (eds) Verhandlungen der Deutschen Gesellschaft für Neurologie 5, Springer Berlin Heidelberg New York London Paris Tokyo Hong Kong, pp 1161–1163
8. Sumner A, Said G, Idy I, Metral S (1982) Syndrome de Guillain-Barré. Effects électrophysiologiques et morphologiques du sérum humain introduit dans l'espace endoneural du nerf sciatique du rat. Résultants préliminaires. Rev Neurol (Paris) 138, 1:17–24
9. Wiethölter H (1989) Verlaufsformen der experimentell-allergischen Neuritis. Springer, Berlin Heidelberg New York London Paris Tokyo
10. Wollinsky KH, Mehrkens H-H, Hülser P-J, Weindler M, Geiger P, Matzek N, Kornhuber HH (1989) Liquorpherese, Liquorfiltration als neues Therapieverfahren bei der Behandlung eines schweren Guillain-Barré Syndroms. Anaesthesist 38 Suppl 1:630