Correspondence

TIZANIDINE VS. BACLOFEN IN THE TREATMENT OF SPASTICITY IN PATIENTS WITH MULTIPLE SCLEROSIS RE: Can. J. Neurol. Sci. 1988; 15:15-19.

To the Editor:

Further study of the tolerance data revealed a slight discrepancy from what we reported in the above publication. In that publication we understated the superior tolerance of tizanidine. Although the efficacy of baclofen appeared to be greater than tizanidine, as judged by physicians and physiotherapists, tolerance of tizanidine was actually superior. We erred in stating that tolerance of baclofen was superior. Although the patients themselves could not perceive a difference in drug tolerance between tizanidine and baclofen, both the investigators and physiotherapists ascertained a significant margin which was significantly in favour of tizanidine (see Table).

Tolerance Assessment+

	Poor**	Fair	Good	Excellent	Comparison Between Groups*
TIZANIDINE					
Patient	14(24%)	13(22%)	21(36%)	10(17%)	N.S.
Investigator	11(19%)	15(26%)	23(40%)	9(16%)	#
Physiotherapist	11(19%)	21(37%)	15(26%)	10(18%)	#
BACLOFEN					
Patient	22(35%)	10(16%)	19(31%)	11(18%)	N.S.
Investigator	23(38%)	6(10%)	28(46%)	4(6%)	#
Physiotherapist	22(36%)	10(16%)	16(26%)	13(21%)	#

\+ Data are expressed as number of patients and % of total population.
* N.S. = not significant
\# $p<0.05$
** The numbers include those who dropped out of the study because of adverse reactions (tizanidine 4; baclofen 11)

This doesn't change the essential statement of our study. Both drugs are useful adjuncts in the treatment of spasticity in patients with multiple sclerosis, with slightly different side effects.

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EFFECT OF BILE DUCT LIGATION-INDUCED LIVER DAMAGE ON THE BLOOD-BRAIN BARRIER

To the Editor:

The homeostasis of the CNS is to a great extent controlled by the blood-brain barrier (BBB). Since BBB integrity is maintained by astrocytes,[1] and since astrocytes are abnormal in hepatic encephalopathy,[2] one would predict that the BBB would also be abnormal in this disease. Evidence from the literature shows BBB dysfunction certainly occurs in acute, severe hepatic encephalopathy. Whether it also occurs in chronic disease, is uncertain, since the evidence is contradictory. The biliary obstruction model of liver damage in the rat represents a disease that is intermediate between acute and chronic.[3] Biliary obstruction was induced in male Wistar rats by ligating the common bile duct using the surgical procedure described by Franco et al.[3] Control rats were sham-operated using the same procedure but without ligation and cutting of the bile duct.

Two to three weeks following surgery the animals were anesthetized, the thoracic cavity was opened and 100 mg/kg of horseradish peroxidase (HRP) (Type II, Sigma Chemical Company, U.S.A.), dissolved in 0.9% saline solution (100 mg/ml) injected into the left ventricle of the heart. The animals were decapitated 30 seconds thereafter. Short-term HRP circulation was used for two reasons; a) to avoid spread of extravasated HRP away from the leakage sites and consequent merging of areas positive for reaction product and b) to avoid the allergic reaction to HRP that occurs in most rats. The left cardiac ventricle was chosen as the injection site in order to deliver HRP to both cerebral hemispheres and to the cerebellum. A maximum of 45 seconds elapsed between opening the thoracic cavity and decapitation. The brief anoxia produced by this procedure does not cause BBB damage.

Brains were carefully removed from the cranial cavities and bisected sagittally. Care was taken to avoid traction on the blood vessels. The non-specific permeability of the BBB in the parieto-occipital cortex and cerebellum was assessed by a) measuring the peroxidase activity in supernatants from tissue homogenates using a spectrophotometric technique,[4] and b) measuring the density of leakage sites in thick sections of the contralateral hemisphere reacted for peroxidase activity.[5] For histological studies, paraffin sections of brain and of liver were stained with phloxine and saffron.

The bile duct-ligated rats weighted only 70% of the body weight of control and sham-operated rats ($p<0.01$). The ligated rats were lethargic and jaundiced. Their livers, common bile ducts and spleens were dramatically enlarged and their abdominal cavities frequently contained clear xanthochromic fluid. The livers were hard on palpation and of yellow hue. Microscopic examination of the liver tissue revealed that the ligation of the bile duct had resulted in a pronounced proliferation of the intrahepatic bile ducts, single cell necroses and abundant mitoses, accompanied by a chronic inflammatory cell infiltrate and, on occasion, by inconspicuous fibrosis.

No differences in either total HRP activity or leakage site density were found between experimental (n=20) and control groups (n=19), showing that this model of liver disease does not cause defects in the blood-brain barrier. Furthermore, no structural abnormalities were seen in the astrocytes or other tissue elements in the cerebral hemispheres or cerebellar parenchyma from the experimental or sham operated groups. Although our histological examination does not rule out functional abnormalities, the normal appearance of both the BBB and astrocytes in this disease, is consistent with the putative role of astrocytes in barrier maintenance.

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