3 Van Dam AP. Diagnosis and pathogenesis of CNS lupus. *Rheumatol Int* 1991;**11**:1–11.
4 Rosenblum MK. Paraneoplasia and autoimmunologic injury of the nervous system: the anti-Hu syndrome. *Brain Pathol* 1993;**3**: 199–212.
5 Baldwin L, Henderson A. Paraneoplastic limbic encephalitis presenting as acute viral encephalitis. *Lancet* 1992;**340**:373.

Lamotrigine control of idiopathic trigeminal neuralgia

Carbamazepine is the drug of choice for idiopathic trigeminal neuralgia, being effective initially in 75% of patients; no other available drug is as effective,[1] although pimozide and oxcarbazepine may be superior.[2] Unfortunately, up to one third of patients cannot tolerate the drug in the doses required to alleviate the pain,[1] and carbamazepine may cause aplastic anaemia, agranulocytosis, and hypersensitivity reactions.[3] Carbamazepine may control idiopathic trigeminal neuralgia by suppressing Na^+ currents either in the trigeminal caudal nucleus or, alternatively, in the gasserian ganglion.[2] Recently, a novel antiepileptic drug lamotrigine has become available, and this is at least as potent as carbamazepine in inactivating Na^+ currents,[4] with fewer side effects. A search of the medical literature did not disclose previous studies of lamotrigine effects on idiopathic trigeminal neuralgia. Thus we obtained authorisation to prescribe lamotrigine in four patients with idiopathic trigeminal neuralgia, from whom informed consent was obtained.

Patient 1, a 55 year old man, developed typical idiopathic trigeminal neuralgia paroxysms in the second right trigeminal branch. Oral carbamazepine (200 mg twice daily) almost completely controlled the paroxysms. In view of possible complicating side effects, the patient accepted the switch to lamotrigine. Carbamazepine was then stopped and replaced with lamotrigine on the following day (at which time the paroxysms had recurred) at 50 mg once a day by mouth, increased by 50 mg aliquots each day. At 100 mg, paroxysms were controlled to a large degree, and relief grew to complete control at 100 mg three times a day. No adverse effects have been seen over six months.

Patient 2 was a 31 year old woman who developed typical idiopathic trigeminal neuralgia attacks involving the first three right branches. Carbamazepine at 200 mg twice a day almost completely controlled the paroxysms, with some attendant somnolence. At 600 mg daily, control was complete, but the patient was severely ataxic and could not drive. Discontinuation of treatment resulted in relapse. Lamotrigine produced complete relief at 400 mg in divided doses, without side effects, over six months.

Patient 3, a 75 year old woman, developed typical idiopathic trigeminal neuralgia in 1973 in the first and second left branches. Carbamazepine was effective only at 2000 mg (complete relief), with considerable side effects. Alcohol injection of the gasserian ganglion gave complete remission for three years. Subsequent recurrences were again treated with alcohol injection, but relief was always shorter. Glycerol injection was effective for four months. Idiopathic trigeminal neuralgia recurred. There were no sensory deficits or dysaesthesiae. Lamotrigine, begun as for patient 1, gave 90% relief at 150 mg three times a day by mouth. After two months, however, the economic burden on the patient led to Fogarty percutaneous compression of the gasserian ganglion, with analgesia at short term follow up.

Patient 4 was a 72 year old man who had frequent attacks of idiopathic trigeminal neuralgia in the left second and third branches for a few months. A sense of burning in the gums was reported lately. Notably, 50% of the attacks presented at night. Speaking and chewing triggered intolerable pain. Carbamazepine at 200 mg twice a day initially controlled the attacks, but very soon produced cardiovascular intolerance. Carbamazepine was replaced with lamotrigine and attacks were completely controlled at 400 mg in divided doses over four months.

Lamotrigine may cause initial ataxia, diplopia, nausea, vomiting, and blurring of sight in 15–35% of the patients treated for epilepsy, but these disappear or are much reduced after dose adjustments.[5] An allergic skin rash is seen in 3–17% of the patients. This can be reduced to no more than 10% if the drug is started at 50 mg once a day for two weeks, increased to 50 mg twice daily for another two weeks, and then brought to a maintenance dose of 200–400 mg in divided daily doses.[5] A similar regimen may be applied for idiopathic trigeminal neuralgia, although we selected a much faster dose increase schedule for rapid control. Doses of lamotrigine can be as high as 1300 mg daily. Carbamazepine and phenytoin speed up the elimination of the drug, whereas valproate slows it.[5]

Lamotrigine is a potent antiglutamatergic agent.[4] Depression of excitatory transmission in the trigeminal caudal nucleus is believed to be part of the range of action of anti-idiopathic trigeminal neuralgia drugs,[6] and thus lamotrigine relief of idiopathic trigeminal neuralgia may not necessarily be due to Na^+ current inactivation.[2]

Our preliminary data require confirmation with a placebo controlled study.

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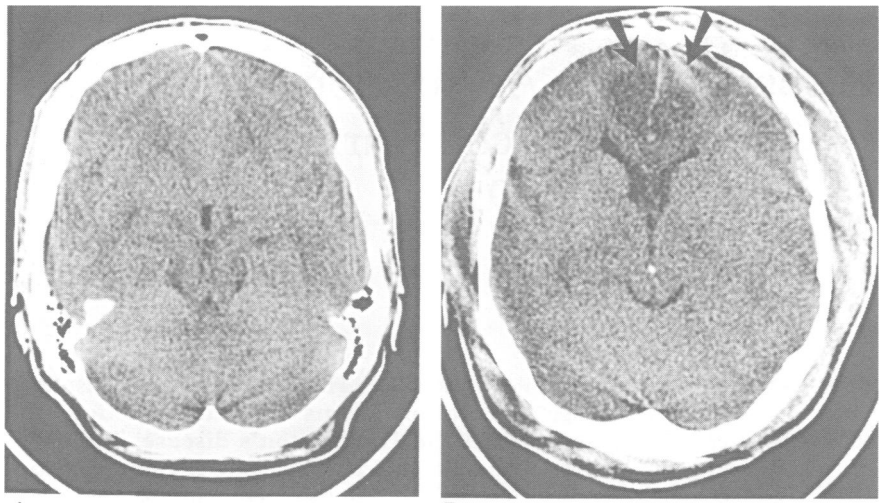
1 Victor M, Martin JB. Diseases of the cranial nerves. In: Braunwald E, Isselbacher KJ, Petersdorf RG, Wilson JD, Martin JB, Fanci AS, *Harrison's principles of internal medicine.* 11th ed. New York: McGraw-Hill 1987;2035–40.
2 Canavero S, Bonicalzi V, Pagni CA. The riddle of trigeminal neuralgia. *Pain* 1995;**60**: 229–31.
3 Rall TW, Schleifer LS. Drugs effective in the therapy of epilepsies. In: Goodman-Gilman A, Goodman LS, Rall TW, Murad F, eds. *Goodman and Gilman's the pharmacological basis of therapeutics.* 7th ed. London: McMillan, 1985;446–72.
4 Meldrum BS. Pharmacology and mechanisms of action of lamotrigine. In: Reynolds EM. *Lamotriginem—a new advance in the treatment of epilepsy.* RSMS international congress and symposium series Nr 204. London: Royal Society of Medicine Services, 1993.
5 Pisani F. La lamotrigina nella terapia antiepilettica: "Focus" sui criteri per un corretto schema posologico. *Presse medicale (Ed It)* 1985;**XII**(suppl 1):1–8.
6 Fromm GH, Chattha AS, Terrence CF, Glass JD. Role of inhibitory mechanisms in trigeminal neuralgia. *Neurology* 1981;**31**: 683–7.

Clinical evaluation of vasospasm in subarachnoid haemorrhage by in vivo microdialysis

Patients in whom subarachnoid haemorrhage is complicated by vasospasm are at risk of developing cerebral infarction. Predicting such a complication may, unfortunately, be difficult. Animal experiments have shown that cerebral ischaemia is associated with raised extracellular glutamate concentrations, which can be measured by in vivo microdialysis. We report on a patient with subarachnoid haemorrhage in whom extracellular glutamate was monitored, by in vivo microdialysis, for four hours every day for four days after operation.

A 38 year old farmer reported to the hospital with a five day history of severe frontal headaches, nausea, and vomiting. Before admission he had had an episode of right sided mild weakness lasting for 24 to 48 hours. He also complained of photophobia and mild neck stiffness. Except for the neck stiffness no focal neurological findings were evident on examination. Lumbar puncture showed a bloody CSF and a subarachnoid haemorrhage was confirmed on cranial CT. A four vessel angiogram disclosed two large separate wide necked aneurysms on the right anterior communicating artery projecting superiorly and inferiorly. Surgery was complicated by intraoperative rupture of the superior projecting aneurysm during the application of the aneurysmal clips. An intracranial Codman bolt was inserted over the right frontal lobe for microdialysis. Intracerebral microdialysis was performed as previously described[1] after stabilisation of the patient in the intensive care unit. The extracellular glutamate reading for day 1 was 298·09 (19·9) μmol/l. This was "high" in comparison with the baseline normal in humans (20–25 μmol/l) as previously reported.[2] An angiogram one day later showed severe focal vasospasm (no filling) of the right anterior cerebral artery. Subsequent CT showed bilateral frontal hypodensities suggesting ischaemic changes (fig 1). The early severe focal vasospasm suggested possible vascular injury related to the aneurysm clip. At the time of the initial study, the patient was very drowsy. The samples on day 2 disclosed a significant decrease in the glutamate concentration to 117·43 (5·86) μmol/l. This correlated with an improvement in the level of consciousness in the patient. On day 3 there was some increase in drowsiness, possibly related to generalised vasospasm and impending bifrontal ischaemia. The microdialysis fluid collections on this day also showed a significant increase in extracellular glutamate concentrations, to 242·53 (19·71) μmol/l. On day 4 clinical state improved with the patient being fully awake. The microdialysis recordings during this time showed a progressive decline in the glutamate concentrations to 42·13 (3·77) μmol/l (see fig 2). The study was approved by the medical ethics committee on human experimentation at the University of Saskatchewan and informed consent was obtained before the study.

Glutamate is an important neurotransmitter. The increase in extracellular glutamate in cerebral ischaemia has been well documented in small animals with the use of in vivo microdialysis[3] and a similar ischaemia induced glutamate response has also been seen in the human brain.[2 4] This increase in glutamate may be important in the development of selective neuronal damage and cere-



A B

Figure 1 CT showing bilateral frontal hypodensities. (A) day 1; (B) day 3 (arrows).

bral infarction. The development of vasospasm with cerebral infarction remains a significant problem in patients with subarachnoid haemorrhage.[5] Unfortunately, identifying patients who may develop cerebral infarction remains difficult. Assessment of vasospasm requires sequential transcranial Doppler studies. At the present time MR angiography is not of high enough resolution to detect arterial size sequentially with any degree of accuracy. The higher complication rates prohibit the routine repetitive use of cerebral angiography. An early warning system, identifying patients at an increased risk for such complications, would prove extremely useful. In our opinion, the use of microdialysis (monitoring several hours every day) seems an alternative way of assessing impending cerebral ischaemia in patients developing vasospasm. The availability of a Codman bolt ensures access for sampling at any time should complications develop in patients with subarachnoid haemorrhage. This technique could potentially be extended for use in patients with head injury (to monitor the development of secondary ischaemia) and in other unstable neurosurgical situations. In our patient, the use of microdialysis showed a good correlation between the deterioration in clinical state, vasospasm, cerebral ischaemia, and raised glutamate concentrations. The values of glutamate were available to us within four to six hours after collection. The observed glutamate pattern over days 1 to 4 suggests that glutamate "signals" cerebral ischaemia before the development of infarction. Faster determinations of the glutamate (or other neurotransmitters and related substances) would prove very useful in managing patients with subarachnoid haemorrhage or other conditions with a propensity to cerebral ischaemia.

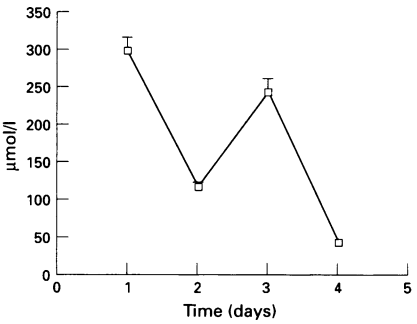


Figure 2 Extracellular glutamate concentrations during the four days of recordings. Values are means (SEM).

In conclusion, we report on a patient with subarachnoid haemorrhage in whom the extracellular cerebral glutamate concentration was measured with in vivo microdialysis for four days after operation. There was a good correlation between the development of vasospasm, the clinical state, and the extracellular glutamate concentrations. In vivo microdialysis may be a useful predictive tool in labile cerebral ischaemic situations. The use of microdialysis in patients with subarachnoid haemorrhage may be useful in the early detection of vasospasm and evolving cerebral ischaemia or infarction.

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1 Kanthan R, Shuaib A, Goplen G. Miyashita H. A new method of in-vivo microdialysis of the human brain. *Journal of Neuroscience Methods* 1995 (in press).
2 Kanthan R, Shuaib A, Griebel R, Miyashita H. Intracerebral human microdialysis: In vivo study of an acute focal ischemic model of the human brain. *Stroke* 1995;**26**:870–3.
3 Mitani A, Andou Y, Matsuda S, Arai T, Sakanaka M, Kataoka K. Origin of ischemia-induced glutamate efflux in the CA1 field of the gerbil hippocampus: an in vivo brain microdialysis study. *J Neurochem* 1994;**63**: 2152–64.
4 Hillered L, Persson L, Ponten U, Ungerstedt U. Neurometabolic monitoring of the ischemic human brain using microdialysis. *Acta Neurochir* 1990;**102**:91–7.
5 Mohr JP, Kistler JP, Fink ME. Intracranial aneurysms. In: Barnett HJ, Mohr J, Stein B, Yatsu JM, eds. *Stroke: pathophysiology, diagnosis and management*. New York: Churchill Livingstone, 1993;645–70.