coding region polymorphisms investigated previously, we assessed the role of two promoter mutations but found no evidence of association. These findings suggest that *PON1* genotypes may not be predictive of PD, although there remains the possibility of interactions with pesticide exposures. Considerably larger studies will be required to investigate such interactions.

Acknowledgements

The authors would like to thank the PD patients and control subjects that participated in this study, Ms Janet Petersen for administering the questionnaire to study subjects, and the neurologists of GHC and UW for referral of PD cases, in particular Drs Robert Gotshall, Ann Hunt, Erik Kraus, Richard Mesher, Steve Pugh, Bruce R Ransom, Ali Samii, Timothy Scearc, Kurt Seiffert, Ken Uchino, Thurman Wheeler.

Funding: this research was supported by National Institute for Environmental Health Sciences Grants ES-04696, 10750, 07033, 09601, 07032 and Environmental Protection Agency Grant 826886–02.

Competing interests: none declared.

S N Kelada, P Costa-Mallen, H Checkoway, H A Viernes, F M Farin, T Smith-Weller, G M Franklin, L G Costa
Department of Environmental Health, University of Washington, Seattle, USA

H Checkoway, W T Longstreth Jr
Department of Epidemiology, University of Washington

C E Furlong, G P Jarvik
Department of Genome Sciences, University of Washington

C E Furlong, G P Jarvik
Department of Medicine, Division of Medical Genetics, University of Washington

W T Longstreth Jr, P D Swanson
Department of Neurology, University of Washington

L G Costa
Department of Pharmacology and Physiology, University of Roma La Sapienza, Rome, Italy

Correspondence to: Dr L G Costa, Department of Environmental Health, University of Washington, 4225 Roosevelt Way, NE, Suite 100, Seattle, WA 98195–6099, USA; lgcosta@u.washington.edu

References

1 **Kondo I**, Yamamoto M. Genetic polymorphism of paraoxonase 1 (PON1) and susceptibility to Parkinson's disease. *Brain Res* 1998;**806**:271–3.
2 **Taylor MC**, Le Couteur DG, Mellick GD, *et al*. Paraoxonase polymorphisms, pesticide exposure and Parkinson's disease in a Caucasian population. *J Neural Transm* 2000;**107**:979–83.
3 **Akhmedova S**, Anisimov S, Yakimovsky A, *et al*. Gln –> Arg 191 polymorphism of paraoxonase and Parkinson's disease. *Hum Hered* 1999;**49**:178–80.
4 **Akhmedova SN**, Yakimovsky AK, Schwartz EI. Paraoxonase 1 Met–Leu 54 polymorphism is associated with Parkinson's disease. *J Neurol Sci* 2001;**184**:179–82.
5 **Wang J**, Liu Z. No association between paraoxonase 1 (PON1) gene polymorphisms and susceptibility to Parkinson's disease in a Chinese population. *Mov Disord* 2000;**15**:1265–7.

Multifocal myoclonus secondary to tranexamic acid

Myoclonus is characterised by sudden and brief involuntary movements. We describe a patient who developed myoclonus and altered mental status following tranexamic acid overdose. The patient was a 61 year old man on chronic ambulatory peritoneal dialysis for adult polycystic kidney disease and had been prescribed lisinopril and metoprolol for long standing hypertension. He presented to hospital because of bloody effluent from his peritoneal catheter. Examination did not reveal any neurological abnormalities. Haemoglobin level was 6.2 g/dl, calcium 2.28 mmol/l, urea 20.3 mmol/l, and creatinine 1109 μmol/l, which was similar to the values taken one month before in the outpatient clinic (urea 20.2 mmol/l and creatinine 1112 μmol/l). Blood and peritoneal fluid were taken for microbiological analyses and were unrevealing.

He was transfused two units of packed cells and started on oral tranexamic acid 500 mg four times daily in order to reduce the bleeding. Six days later he became dull and developed spontaneous, arrhythmic, and multifocal myoclonus. On repeat renal function testing, the urea and creatinine levels were 20.6 mmol/l and 1190 μmol/l, respectively. An ECG and urgent brain computed tomography were unremarkable but an electroencephalogram (EEG) showed intermittent spike waves over both parasagittal regions. No other cause of epilepsy was found. Anticonvulsants were not started as it was felt that the involuntary movements were not disabling and likely to be a transient adverse drug effect. Four days after tranexamic acid had been stopped, the patient had regained his premorbid mental state and the myoclonus had ceased. Normal posterior dominant alpha activity was recorded on a repeat EEG, without further epileptiform discharges. Six months after this event the patient remains free from seizures.

Comment

Drug induced myoclonus usually occurs with encephalopathy and is often a diagnosis of exclusion. In addition, other neurological signs such as ataxia, coma, generalised seizures, and headache may be present with certain agents. Implicated drugs include antibiotics, anaesthetics, calcium channel blocking drugs, antidepressants, and antiepileptic drugs. Tranexamic acid (TAMCA; 4-(aminomethyl)cyclohexanecarboxylic acid) is commonly used in the treatment of disorders that predispose to bleeding. It is a synthetic lysine analogue that has strong antifibrinolytic activity. Plasminogen binds to fibrin to form plasmin, which in turn degrades fibrin into fibrin degradation products. TAMCA blocks the lysine binding site on plasminogen and prevents interaction with fibrin. Clinical trials have shown that TAMCA reduces blood loss in patients with primary menorrhagia, and in those undergoing cardiopulmonary bypass, prostatectomy, hip replacement, and liver transplantation.

TAMCA is generally well tolerated. Side effects are mainly gastrointestinal, such as nausea, vomiting, diarrhoea, and abdominal pain. There are, however, experimental studies of neurotoxicty.[1–4] Direct application of TAMCA to the cortex of cats produces spike-wave bursts on EEG similar in appearance to that found in feline generalised epilepsy.[4] The ability to elicit epileptic activity depended on the concentration of the drug and the area of cortex exposed. Intravenous injection causes intracranial and systemic hypertension as well as epileptiform discharges on the EEG.[3] Drugs may induce seizures by modulating neurotransmission, as application of excitatory transmitters such as kainic acid and inhibitory receptor blockers such as penicillin have been shown to evoke seizures. By applying TAMCA to the spinal cord of rats, Furtmüller was able to demonstrate a dose dependent hyperexcitibility.[5] This is blocked by the addition of muscimol, a γ-aminobutyric acid (GABA) receptor agonist, which indicates that tranexamic acid induces convulsions by blocking inhibitory GABAergic neurotransmission.

Clinically, an increase in cerebral ischaemia has resulted when TAMCA has been given for the treatment of subarachnoid haemorrhage.[3] TAMCA induced seizures have been reported in a man who was inadvertently given a 50 mg intrathecal dose during spinal anaesthesia and developed status epilepticus.[6] The patient required thiopentone infusion as the seizures were not controlled with phenytoin and midazolam; the clinical course was complicated by multiorgan dysfunction and critical illness polyneuropathy. Our patient with end stage renal failure was given an accidental overdose of oral TAMCA which resulted in myoclonus that resolved after the drug was stopped. As excretion of this drug depends on renal function, dosage adjustment is required in patients with renal failure; the efficacy of haemodialysis in removing the drug has not been studied. This case suggests that TAMCA overdose should be considered as a cause of drug induced myoclonus.

A C F Hui, T Y H Wong, K M Chow, C C Szeto
Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China

Correspondence to: Dr Andrew Hui; cfhui@cuhk.edu.hk

References

1 **Schlag MG**, Hopf R, Zifko U, *et al*. Epileptic seizures following cortical application of fibrin sealants containing tranexamic acid in rats. *Acta Neurochir* 2002;**144**:63–9.
2 **Fodstad H**. Convulsive seizures following subdural application of fibrin sealant containing tranexamic acid in a rat model. *Neurosurgery* 2001;**49**:479–80.
3 **Yamaura A**, Nakamura T, Makino H, *et al*. Cerebral complication of antifibrinolytic therapy in the treatment of ruptured intracranial aneurysm. Animal experiment and a review of literature. *Eur Neurol* 1980;**19**:77–84.
4 **Pellegrini A**, Giaretta D, Chemello R, *et al*. Feline generalized epilepsy induced by tranexamic acid (AMCA). *Epilepsia* 1982;**23**:35–45.
5 **Furtmüller R**, Schlag MG, Berger M, *et al*. Tranexamic acid, a widely used antifibrinolytic agent, causes convulsions by a gamma-aminobutyric acid(A) receptor antagonistic effect. *J Pharmacol Exp Ther* 2002;**301**:168–73.
6 **De Leede-van der Maarl MGJ**, Hilkens P, Bosch F. The epileptogenic effect of tranexamic acid. *J Neurol* 1999;**246**:843.

Immunohistochemical study of caveolin-3 in idiopathic hyperCKaemia

With the increasing concern about malignant hyperthermia and with the inclusion of creatine kinase determination in the automated blood chemistry profile, performed as part of health screening, the number of subjects with raised serum creatine kinase (hyperCKaemia) without clinical signs of neuromuscular disease is continuously increasing. In 1980 Rowland *et al* coined the term "idiopathic hyperCKaemia" to describe patients with