VALERIES JONES
Consultant in stroke medicine
Mayday University Hospital, Croydon

Aciclovir neurotoxicity is an important side effect of therapy in patients with renal impairment

Editor – We read with interest the article by Bell and colleagues (*Clin Med* June 2009 pp 231–5). They describe aciclovir therapy as essentially safe, highlighting the potential risk of crystal nephropathy. This potentially life-threatening complication is well recognised in nephrology, but not widely publicised, as it is often only evident in the presence of renal impairment. Recognition has implications for all physicians given the prevalence of chronic kidney disease and acute kidney injury. Such concerns might explain five patients not receiving full dose aciclovir in their study.

Aciclovir and latterly valaciclovir are established antiviral agents versus herpes simplex (HSV) and varicella zoster (VZV). Neurotoxic side effects have been described since the early 1980s.[1–3] Such cases often resulted from recommended aciclovir dosing for HSV encephalitis in the context of renal impairment. As approximately 90% of the drug is renally excreted; half-life and serum levels of aciclovir are markedly elevated in renal disease.

A range of symptoms from tremor to coma have been described, with typical onset 24 to 72 hours after both oral and intravenous aciclovir. Visual hallucinations and death delusion are striking features in patients prescribed aciclovir with previously normal brain function (usually for treatment of shingles or as anti-cytomegalovirus prophylaxis).[3] In patients with presumed encephalitis, failure to consider aciclovir neurotoxicity may lead to misinterpretation of neuropsychiatric symptoms as worsening encephalitis; precipitating inappropriate dose increases, rather than reduction or withdrawal.

The exact mechanism is unknown. 9-carboxymethoxymethylguanine (CMMG) is an aciclovir metabolite, present in serum and cerebral spinal fluid. In patients with neuropsychiatric side effects, significantly higher serum CMMG levels have been demonstrated; with stronger symptom correlation than aciclovir.[5] Most affected patients had renal impairment.[5]

To improve the therapeutic regimen aciclovir dosing should always be adjusted for renal function[6] and patients adequately hydrated prior to oral or intravenous administration. Possible aciclovir neurotoxicity should be considered with new neurological symptoms after 24 hours, particularly in the presence of renal impairment. Serum aciclovir measurements require 24 hours in most UK centres and often lag behind clinical signs. Levels might be useful for diagnostic confirmation. Early recognition with appropriate dose changes is crucial. If distinguishing worsening encephalitis from neurotoxicity proves difficult, a trial of haemodialysis might be appropriate.[7]

MARK E BRADY
Specialist registrar in renal medicine

JOHN MAIN
Consultant renal physician
James Cook University Hospital, Middlesbrough

References

1 Wade JC, Meyers JD. Neurologic symptoms associated with parenteral acyclovir treatment after marrow transplantation. *Ann Intern Med* 1983;98:921–5.
2 Cohen SM, Minkove JA, Zebley JW 3rd, Mulholland JH. Severe but reversible neurotoxicity from acyclovir. *Ann Intern Med* 1984;100:920–1.
3 Tomson CR, Goodship THJ, Rodger RSC. Psychiatric side-effects of acyclovir in patients with chronic renal failure. *Lancet* 1985;II:385–6.
4 Haefeli WE, Schoenenberger RA, Weiss P, Ritz RF. Acyclovir-induced neurotoxicity: concentration-side effect relationship in acyclovir overdose. *Am J Med* 1993; 94:212–5.
5 Helldén A, Odar-Cederlöf I, Diener P *et al.* High serum concentrations of the acyclovir main metabolite 9-carboxymethoxymethylguanine in renal failure patients with acyclovir-related neuropsychiatric side effects: an observational study. *Nephrol Dial Transplant* 2003;18:1135–41.
6 Ashley C, Currie A. The renal drug handbook, 3rd edn. Oxford: Radcliffe Publishing, 2009.
7 Beales P, Almond MK, Kwan JT. Aciclovir neurotoxicity following oral therapy: prevention and treatment in patients on haemodialysis. *Nephron* 1994;66;362–3.

Medicine at the sharp end

Editor – We read with interest the article by McNeill and colleagues (*Clin Med* June 2009 pp 214–8) suggesting that benefits from a consultant presence on an acute medical unit (AMU) included greater numbers of same-day discharges and a shorter length of stay. There remains little evidence as to why consultant presence results in these positive outcomes.

We retrospectively audited 145 randomly selected patients admitted via the AMU at the Countess of Chester Hospital NHS Foundation Trust. Patients clerked by a foundation or core medical training grade doctor were then reviewed on the post-take ward round (PTWR) by a consultant or middle grade (specialist registrar (SpR) or staff grade). We studied the number of same-day discharges following the PTWR and accuracy of diagnosis at the PTWR compared with final diagnosis on the hospital discharge summary.

Consultants reviewed 72 patients (mean age 68 years; 33 men) and middle grades reviewed 73 patients (mean age 66 years; 39 men) on the PTWR. Consultants made an accurate PTWR diagnosis in 69 patients (95.8%) which was significantly higher (χ^2, $p<0.0001$) than the middle grades who made an accurate diagnosis in 60 patients (82.2%). The main reason for this difference appeared to be that there was only a documented PTWR diagnosis in 89% of the patients reviewed by middle grades, whereas there was a written PTWR diagnosis in all (100%) of the patients reviewed by consultants. Consultants also discharged higher numbers of patients at the PTWR (17 patients *v* 6 patients; χ^2, $p<0.01$).

Our data confirm that consultant review at PTWR results in a greater number of same-day discharges and suggests that the benefits of a consultant presence on the AMU may be due to the higher rate of accurate initial diagnosis. This seems to be because of an increased willingness of consultants to commit to a written diagnosis. The Joint Royal Colleges of Physicians Training Board curriculum for general (internal) medicine identifies 'developing a problem list and action plan' as a key competency, and we would suggest that trainees should be encouraged to commit to and