
LETTERS TO THE EDITOR

Sir,

We would like to comment on the letter by Davis, Diggory and Seward¹ as we feel that their results are biased and misleading. Acetazolamide is a drug with potentially fatal metabolic consequences.^{2,3} The flaw in their study is the exclusion of patients who may already have sustained a fatal arrhythmia, or who have previously been hospitalised with side-effects requiring cessation of therapy.

Biochemical monitoring is used to screen for two serious consequences of acetazolamide therapy: renal failure^{4,5} and metabolic acidosis.⁵ Exacerbation of mild renal failure is indicated by an increase in creatinine (or even less sensitively urea). Metabolic acidosis is indicated by a reduction in bicarbonate. It has previously been shown that serum sodium and potassium are not significantly altered by acetazolamide therapy.⁶ Acetazolamide produces a hyperchloraemic acidosis with an impairment in H⁺ ion secretion and a consequent loss of K⁺ ions. Hypokalaemia is a late manifestation of acetazolamide toxicity which should not occur if patients have their metabolic state regularly assessed, with a view to cessation of their medication should they become significantly acidotic. Some patients benefit from having concurrent administration of supplemental alkaline therapy without a reduction in drug efficacy.⁷

In approximately 40% of 2000 patients given a trial of long-term carbonic anhydrase inhibitor therapy the drug had to be discontinued because of side effects.⁷ In patients with commonly encountered problems, such as mild renal impairment, chronic respiratory disease or diabetes, or in those taking aspirin, the metabolic acidosis induced may have serious^{4,5,8} or fatal consequences.^{2,3}

We recommend that patients on long-term acetazolamide continue to have regular measurements of creatinine and electrolytes (in particular bicarbonate), with a view to discontinuing therapy should there be any suggestion of incipient renal failure or significant metabolic acidosis.

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References

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Sir,

We are sorry that Mr Barnes finds our study results biased and misleading. We were not looking at short-term electrolyte disturbance, but were interested only in elderly patients who had been receiving long-term acetazolamide (i.e. for >6 months). Few ophthalmology departments routinely measure such patients' electrolytes when they attend clinic and our study was aimed at answering the question as to whether or not this was acceptable practice. Patients who had sustained a fatal arrhythmia or had had their therapy withdrawn because of earlier side effects were not included. We found no significant difference in potassium, sodium and urea between the patients using acetazolamide and an age- and sex-matched control group who were not using acetazolamide.

Mr Barnes' argument, based mainly on case reports, would seem to suggest that we should routinely measure bicarbonate to screen for the development of acidosis. Most hospitals, including the Chelsea and Westminster, no longer offer routine measurement of venous bicarbonate. This is because

bicarbonate measurement (strictly total CO₂ as bicarbonate cannot be readily measured) is rarely clinically indicated and is expensive. In addition it deteriorates in transit and routine measurement of venous samples is likely to be misleading.¹ An accurate assessment of a patient's acid-base status requires measurement of pH and PCO₂ and is, therefore, usually performed on arterial samples when clinically indicated.

Regular routine estimation of plasma electrolytes on patients receiving acetazolamide is not practised by most ophthalmology departments and our study found no need for regular potassium estimation. We believe ophthalmologists will demand more evidence-based medicine in the form of prospective studies of the acid-base status in elderly patients before advocating regular arterial samples to assay bicarbonate in ophthalmology clinics.

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Sir,

I read with interest the recent report by Fraser and Horgan of meningococcal meningitis associated with unilateral subretinal and vitreous haemorrhage.¹ This is not the sole documented case as I have also reported on a patient with meningococcal meningitis in whom intraocular haemorrhage occurred.² In this case, bilateral intraretinal haemorrhages developed in addition to unilateral petechial iris haemorrhages and sectorial haemorrhagic iris infarction. In contrast to Fraser and Horgan's case, this latter case was quite clearly related to meningococcal septicaemia and disseminated intravascular coagulation. Cutaneous and systemic haemorrhages in meningococcal septicaemia are considered to occur by different mechanisms. While cutaneous purpura is the result of an endotoxin- and immunologically-related occlusive vasculitis (in which bacteria may thrive), disseminated intravascular coagulation is the main cause of the sterile systemic haemorrhages.^{3–5} Thus, although initial management of intraocular haemorrhages in meningitis may be conservative, as suggested by Fraser and Horgan, particularly when associated with *Neisseria meningitidis*, a concerted effort must be made to exclude potentially fatal disseminated

intravascular coagulation, even in the absence of cutaneous purpura.

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Sir,

We are grateful for Dr Kennedy's interest in our paper¹ and his comments are highly pertinent.

It is undoubtedly very important that disseminated intravascular coagulation is excluded in meningococcal meningitis, and any patient noted to have an intraocular haemorrhage in the acute stages of the disease should be investigated appropriately. However, retinal or vitreous haemorrhage may be difficult to diagnose in the acute situation. The patient often has a decreased level of consciousness and therefore will not complain of a decrease in vision. Examination of the fundi can also be difficult because of photophobia and the problems of dilating a patient who is undergoing neurological observations.

The patient who we reported did not complain of any visual problems until 6 days after her admission, and this seems to be typical of ocular complications in meningitis. Dr Kennedy's case exemplifies the importance of ocular examination in the patient with meningococcal meningitis at the time of presentation – and this examination should continue throughout the course of the disease. Further to this, because ocular complications of meningitis may be as high as 70%,² there may well be a case for routine referral to an ophthalmologist for a fuller examination once the acute stage of the disease has passed.

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