induced adrenal suppression as part of his terminal illness. He did have a history of disseminated cytomegalovirus infection which can be associated with adrenal failure and acute Addisonian crisis in patients with AIDS. A post-mortem was not obtained to study the adrenal tissue, but the temporal association of the adrenal failure with administration of fluconazole makes us feel that it was the causative factor. The ketoconazole is unlikely to have affected the adrenals as it was discontinued 38 days prior to the development of the adrenal insufficiency.

In light of this, we feel that it is prudent to recommend that patients being treated with fluconazole should be monitored for the onset of signs and symptoms consistent with adrenal insufficiency.

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References

Changes in AVP following aggressive diuretic therapy of severe congestive cardiac failure in elderly patients

Sir,

Congestive cardiac failure (CCF) is a progressive disorder and is associated with a high mortality, particularly in more advanced stages. Clinical, non-invasive and invasive methods used in the assessment of heart failure are unreliable. Plasma arginine vasopressin (AVP) levels have been shown to rise in CCF and fall towards normal after successful treatment, reflecting part of the neurohormonal response to cardiac failure whose purpose is to restore circulatory homeostasis.

In a prospective study of 13 elderly patients (aged 75–90 years) with New York Heart Association (NYHA) Class 3 and 4 CCF, we assessed the changes in plasma AVP levels which occurred during aggressive diuretic therapy over a period of 7 days. Changes in plasma AVP levels in 13 age and sex matched normal subjects were also determined over the same period. Prior to the study, patients were all being treated with frusemide (mean daily dosage 40 mg), amiloride (mean daily dosage 5 mg), and 6 patients were on digoxin therapy (mean daily dosage 0.10 mg). None was being treated with angiotensin converting enzyme inhibitors.

Pretreatment samples for urea, electrolytes, creatine and AVP were taken and the CCF patients were commenced on oral frusemide combined with metolazone (mean daily dosages 70 mg and 6.25 mg respectively). Dosages were adjusted daily according to clinical changes and biochemistry.

At the end of the study period, all patients with CCF had improved clinically and symptomatically with a mean weight loss of 6 kg ($P = 0.0001$). Mean plasma creatinine increased from 104.9 to 120.8 pmol/l, but there were no other significant biochemical abnormalities. Mean plasma AVP fell from 4.13 pmol/l to 2.07 ($P = 0.005$) in the CCF group, but was unchanged (0.83 vs 0.97; $P = 0.805$) in normal subjects over the same period. It is notable that those patients initially classified as NYHA class 4 displayed a very wide range of AVP levels (1.1–12.9 pmol/l), with 4 of these having levels greater than 8 pmol/l.

High plasma AVP levels in CCF are associated with lower cardiac indices, elevated plasma renin, adrenaline and aldosterone levels, all of which may indicate a relatively poor prognosis. We conclude therefore that within the category of severe heart failure as assessed by the NYHA classification there lies a subgroup of patients with a more unfavourable prognosis who may require prolonged aggressive therapy and more frequent follow-up. Plasma AVP levels provide a non-invasive means of identifying these patients.

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