LETTERS TO THE EDITOR

Symptomatic salicylate ototoxicity: a useful indicator of serum salicylate concentration?

Sir: I read with interest the article by Halla, Atchison, and Hardie.1 We have recently studied the kinships of salicylate in elderly patients with osteoarthritis and rheumatoid disease who were taking benorylate and compared them with a group of young healthy volunteers.2 Although the mean renal clearance of total salicylic acid was significantly lower in the elderly arthritic patients, the adverse effects of tinnitus and deafness were less common in this age group. In contrast, the elderly frequently developed vague symptoms, such as anorexia, sweating, and reduced mobility, which were not immediately recognisable as manifestations of salicylate toxicity. Our findings support the conclusion of Halla et al. that symptomatic ototoxicity is too non-specific and insensitive to be a clinically useful indicator of salicylate concentration. Nevertheless, the development of non-specific symptoms may be the only indicators of significant salicylate toxicity. On the basis of our results, we would recommend a reduction of the starting dose of salicylate in elderly patients and plasma sampling for salicylate concentrations in individual patients in whom there is the slightest suspicion of salicylate toxicity.

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Plasma endothelin-1 concentrations in polyarteritis nodosa

Sir: Endothelin-1 is a new, endothelium derived, vasoactive peptide with the most potent vasoconstrictive effect known to date.1 Recent accumulating evidence suggests that endothelin-1 may play an important part in vascular disorders.2 Polyarteritis nodosa is a systemic necrotizing vasculitis characterised by inflammation and necrosis of small and medium sized muscular arteries.3 Vascular endothelial growth factor might have an important role in the pathophysiology of polyarteritis nodosa, and thus we measured circulating levels of endothelin-1 in patients with polyarteritis nodosa.

Plasma concentrations of endothelin-1 were measured by radioimmunoassay using polyclonal antibody (sensitivity 0-2 pg/tube) after plasma extraction on C2 ethyl microcolumn (Amersham). Angiotensin 2, another endothelial cell damage marker, was also measured by radioimmunoassay (sensitivity 0-2 pg/tube) after plasma extraction by ethanol. Two groups of subjects were studied. Group 1 included six men and eight women, aged 52 (11) years (mean (SE), with recently diagnosed polyarteritis nodosa,4 and normal renal function and arterial blood pressure. Group 2 included 14 normal subjects matched for age and sex. The mean (SE) plasma concentration of endothelin-1 in group 1 patients (4.23 (0.4) pg/ml (range 3.77) was not significantly different from that of group 2 patients (3.8 (0.3) pg/ml). Similarly, the mean (SE) plasma concentration of angiotensin 2 in group 1 patients (141 (37) pg/ml was not different than that of group 2 patients (100 (15) pg/ml (Student's t test).

An increase in plasma endothelin-1 has been reported in numerous conditions where vasospasm is a predominant factor, such as Raynaud's phenomenon,5 arterial pulmonary hypertension,6 or umbilical artery vasospasm.4 The absence of significant increases in plasma endothelin-1 or angiotensin 2 in patients with polyarteritis nodosa may be explained by the different processes occurring. In polyarteritis nodosa, when arterial blood pressure and renal function are normal, complications are more often associated with thrombosis than vasospasm. Pathological findings, such as fibrinoid necrosis or inflammatory mononuclear cell infiltrates, are usually segmented and located in the media of small and medium sized arteries, and may not affect endothelial cells. Intimal proliferation and later intimal fibrosis may appear without excessive production of endothelin-1 by endothelial cells.

Our data suggest that endothelial cell damage, as represented by excessive production of endothelin-1, is not a predominant factor in the pathophysiology of polyarteritis nodosa.

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Patients' profiles

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<th>Case No</th>
<th>Age (years)</th>
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<th>Predisposing factor</th>
<th>Assay temp (°C)</th>
<th>ESR* (mm/h)</th>
<th>Duration of symptoms (days)</th>
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<td>38.2</td>
<td>62</td>
<td>75</td>
<td>Mycobacterium tuberculosis</td>
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</tbody>
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*ESR=erythrocyte sedimentation rate.