OTOTOXICITY OF GENTAMICIN IN THE ELDERLY

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Advancing years and exposure to aminoglycoside therapy are each associated with deafness. Are then elderly patients at greater risk of sustaining a hearing loss than younger patients exposed to an equivalent insult in terms of the serum aminoglycoside concentration/time profile?

Ten courses of Gentamicin treatment, administered by intermittent injection, were monitored in nine patients, aged 80 to 88 years. One patient received a second course two months after the first. Three pairs of blood samples were taken for Gentamicin assay, the first sample of each pair being taken immediately before a dose, the second one hour after that dose. The initial pair was taken on the second day, the second pair about three days later, and the third near the end of treatment. Maintenance doses were adjusted according to assay results, with particular attention to maintaining the pre-dose concentration below 2 ug/ml, in accordance with current practice. All samples were assayed by the enzyme multiplied immunoassay technique (EMIT). Fluorescent immunoassay produced similar results ($p>0.1$, paired t-test). However, microbiological plate diffusion produced results 18 per cent higher than those obtained by EMIT ($p<0.001$).

Pure tone audiometry was carried out in a sound-treated room by a trained technician, in the first three days and at the end of treatment, with one or more follow-up audiograms in succeeding weeks. In order to minimise demands on the patient only air conduction was tested. Any wax was removed beforehand. A hearing loss of 10 dB or more at two or more frequencies on a given occasion (Davey et al 1982) was considered to be significant. Such losses (average 19 dB) were recorded following six courses of treatment in five patients, only one patient noticing the loss. Psychological ratings remained maximal in relation to three of these courses, improved during two and remained stable for one, suggesting that hearing losses were not artefacts resulting from inability to co-operate. Ototoxicity was associated with an exposure to Gentamicin, expressed in terms of 'baseline' area (see figure),of above 15 µg.days/ml, except in the only patient in whom a reversible loss was documented. An area of upto 45 µg.days/ml appeared safe in Mawer et al's (1974) younger patients. We suggest therefore that the elderly have increased endorgan sensitivity to Gentamicin.

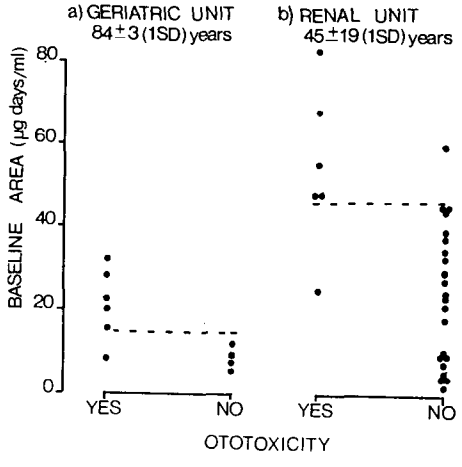

Figure. Relationship between baseline area and ototoxicity. The areas in a) were obtained by multiplying the mean of the measured pre-dose Gentamicin concentrations by the duration of treatment. This method gave results not significantly different from those obtained using Mawer et al's one compartment kinetic model (as had been used in b)). Mawer's group used a microbiological assay, but interassay variation could not have accounted for the 300 per cent difference in threshold for ototoxicity.

Davey, P.G. et al (1982) Br. J. Audiol. 16: 151-154.
Mawer, G.E. et al (1974) Br. J. clin. Pharmac. 1:45-50.