Gentamicin dosage schedules

Sir,

The paper by Yoshioka et al. (Archives, 1978, 53, 334), gives a guide to gentamicin dosage for an age group missed by the popular adult nomograms. Such a guide is necessary when choosing initial dosage, but we believe that subsequent maintenance therapy should be monitored by determining serum gentamicin levels in all patients rather than just in ‘difficult’ cases as suggested by the authors. The disadvantage of determining the half-life of gentamicin from creatinine clearance is that the latter should be corrected to the patient’s lean body mass (Hull and Sarubbi, 1976). The lean body mass of an acutely-ill oedematous child with chronic renal disease is difficult to estimate.

Gentamicin clearance is a sensitive indicator of renal function, and is logically best predicted by measuring serum levels of the drug itself. Sawchuck and Zaske (1976) described a method of calculating the half-life and distribution volume of gentamicin. We have adapted this method for a programmable calculator instead of the computer. Our experience suggests that the one-compartment model used in this method is perhaps too simple: the half-life derived from serum levels of gentamicin in the first 4 hours after a dose overestimates the subsequent rate of clearance and slightly underestimates the interval between doses. A better model could be made by fitting a 2- or 3-term exponential function to later serum levels (Kahlmeter et al., 1978) but the one-compartment model does provide useful insight into the effects of varying dosage regimens.

We question whether a dosage of 1 mg/kg is enough to treat serious infections, especially by IM injection. The peak serum levels achieved in the 3 patients treated by the schedule were all below 5 μg/ml. The longer the dose takes to enter the circulation, the lower the interstitial fluid levels will be (Kozak et al., 1977).

There appears to be no alternative to repeated measurement of serum gentamicin levels, and our efforts should be directed towards improving the accuracy and availability of our assays. Micromethods using small quantities of blood would be particularly valuable for very young children for whom venepuncture is often difficult or impossible. There is one factor in our favour: the interval between doses for many patients with renal failure is longer than our slowest bio-assay.

R. T. MAYON-WHITE and ELIZABETH M. PERKS
Regional Public Health Laboratory and Department of Bacteriology, Radcliffe Infirmary, Oxford

References


Dr Yoshioka and co-workers comment:

We welcome the comments from Dr Mayon-White and Miss Perks. Their opinion is acceptable as a principle that serum levels should be monitored in all patients receiving gentamicin treatment. But unfortunately many hospitals do not provide antibiotic assay systems, and even in hospitals in which this service is available, the reproducibility of measured levels is reported to be poor (Reeves and Bywater, 1975). In such a situation we believe proposed nomograms or other pharmacokinetic data are still a useful guide in planning gentamicin treatment.

The statement about correcting the creatinine clearance value to the patient’s lean body mass seems misleading. Obviously, endogenous creatinine clearance is a value which is determined on the basis of the serum level and the amount of creatinine excreted in urine in a unit of time. Rapid evaluations of creatinine clearance or glomerular filtration rate are proposed on the basis of age, body weight, and serum creatine level for adults (Hull and Sarubbi, 1976), and of body length and plasma creatinine level for children (Schwartz et al., 1976). However, we do not agree with the use of values obtained by these expedients until it is otherwise proved that these values actually correlate with serum half-life of gentamicin. Only values determined in individual patients should be used for our dosage schedule at the present time.

As far as the serum half-life determination of gentamicin is concerned, we do not argue with their statement that it should be done after 4 hours of dosing. However, absorption of gentamicin from the injected site is rapid even in patients with renal insufficiency. Peak levels were attained within 2 hours in all our patients (Table I) after intramuscular dosing, and therefore we do not believe the lower blood level in the 3 patients was due to delayed absorption.

The serum concentration of gentamicin was once reported to be unpredictable (Kaye et al., 1974). But recently it became evident that a series of factors affect the serum concentration. These include obesity of the patient, unstable renal function, haematocrit values, administration of other drugs, or certain disease states of the patient. The accuracy of prediction of gentamicin level was reported to have markedly improved by taking account of these factors (Hull and Sarubbi, 1976). We believe that satisfactory treatment can be achieved, with few exceptions, by using dosage schedules; however, it


References


