Title: VOLUME OF DISTRIBUTION IN PATIENTS WITH GRAM NEGATIVE SEPSIS IN THE I.C.U.

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Introduction. The volume of distribution of drugs administered to patients with life threatening gram negative sepsis is poorly documented and difficult to predict (1). Early peak plasma levels of aminoglycosides ( > 7μg/ml for tobramycin and gentamicin) reflecting volume of distribution, have been shown to be related to survival in non I.C.U. patients with gram negative pneumonias (2). We studied patients in a combined Medical-Surgical I.C.U. to determine

a) if there was a predictable alteration in the volume of distribution of aminoglycosides in patients with gram negative sepsis
b) whether survival in I.C.U. patients was related to initial peak aminoglycoside levels

Methods. We studied 50 patients (with I.R.B. approval and informed consent) in the I.C.U. with sepsis syndrome (3) and cultures growing gram negative organisms sensitive to aminoglycosides. We measured peak aminoglycoside levels thirty minutes after a loading dose of 3mg/kg of gentamicin or tobramycin. We calculated the initial volume of distribution using a standard one-compartment model. We compared the predicted volume of distribution (3) to the calculated volume of distribution. We compared the peak initial aminoglycoside levels in survivors (S) and non-survivors (NS).

Results.

| Volume of Distribution (Liters/kg x ± S.D.) | S (n=29) | N.S.(n=21) |
|---|---|---|
| Predicted | 0.22 | 0.22 |
| Actual VD | 0.30±.07 | 0.32±.11 |
| Peak Aminoglycoside level (mcg/ml x±SD) | 8.79±2.53 | 8.80±1.85 |

The calculated volume of distribution was significantly greater than the predicted value in patients with gram negative sepsis ($p < 0.0005$ Student's paired t test). Survival was not related to the peak initial aminoglycoside level.

Discussion. The calculated volume of distribution was 141% of the predicted value in our patients who had gram negative sepsis. Thus, calculation of loading doses of aminoglycosides in septic patients should allow for this difference in volume of distribution. This difference is presumably related to an increase in extra cellular fluid volume and has important implications for other drugs used in the I.C.U. Contrary to work done in hospitalized non-I.C.U. patients we have demonstrated no relationship between survival and early peak aminoglycoside levels. This may be due to consistently higher levels achieved using a 3mg/kg loading dose or the inability of a single variable to predict outcome in patients with multi-system organ failure in the I.C.U.

References

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