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Is Mannitol Metabolized?*

JOHN KAPP CLARK† AND HAROLD G. BARKER.‡ (Introduced by Carl F. Schmidt.)

From the Departments of Pharmacology and Medicine, and the Harrison Department of Surgical Research, University of Pennsylvania School of Medicine and Hospital, Philadelphia, Pa.

If, as has been recently suggested,[1,2] mannitol is in part disposed of by non-renal means, probably metabolic, it cannot be used as a measure of extracellular fluid space.[3] Such a circumstance would render invalid calculations of glomerular filtration rate in which the rate of infusion is substituted for the rate of excretion, UV, in the clearance formula $C = UV/P$ after the plasma level, P, has become constant,[4] or from the falling curve of plasma concentration without urine collection,[5] if mannitol is used as a test substance. Since the publication of the constant infusion technic for determining renal clearances,[4] we have routinely infused our test solutions, mannitol and para-aminohippurate, from a syringe with a motor driven worm screw, and our data on subjects with relatively normal renal function, in cases where both infusion solutions and urine were analyzed, indicate no extra-renal loss when mannitol recovered in the urine is balanced against that infused. In these tests, a period of one hour, when possible, was allowed for equilibration, urine was collected by catheter with bladder washing and clearance periods were usually 20 minutes or longer. Plasma levels varied from 100 to 50 mg%. Mannitol was determined by a modification[6] of Smith's method[7] in most cases and by the colorimetric method[8] in a few. Total para-aminohippurate was determined by a modification of Smith's method.[9]

Results. Our data are presented in two groups. The first, the unselected series, consists of all patients in whom both urine and infusion solutions were analyzed and contains 92 clearance periods in 29 tests on 22 patients with relatively normal renal function.§

The average urinary recovery of mannitol for all 92 periods was 100.4 mg for every 100 mg injected (range 62 to 156). The standard deviation of this series is 16.7; standard error of the mean 1.74. For the difference 100.4-100.0 the t value is 0.23, indicating that the amount recovered in the urine does not differ significantly from that injected.

In many of the clearances satisfactory mannitol plasma equilibrium was not achieved due to inaccurate preclearance estimation of renal function, a priming dose of improper size, changing renal function, etc. In addition, some periods are inaccurate due to technical difficulties such as obvious urine collection errors, chemical analytical errors, pump

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† National Institute of Health Senior Research Fellow and formerly Research Fellow in Pharmacology.

‡ Harrison Fellow in Surgical Research, and formerly Research Fellow in Pharmacology.

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§ Mimeographed sheets containing data will be furnished on request.

failures, etc. These cases could be excluded, although the fact that their inclusion introduces no significant in-out difference indicates that random rather than systematic errors are involved.

The second group of data, the selected series, consisting of clearance periods chosen on the basis of plasma equilibrium and technical perfection, but, of course, without regard to mannitol recovery, contains 30 periods from 16 tests on 12 patients.§

This series contains only periods preceded and followed by determinations of plasma concentration that did not differ by more than 3.5 mg%, a value within the error of the method (standard deviation = ±2.5 mg%). An actual difference of this magnitude, in 2 specimens drawn 30 minutes apart, would represent, on the basis of an average normal mannitol space of 15 liters,[3] a gain or loss of 17.5 mg/min. and thus might obscure a very large extra renal loss. To determine whether equilibrium had been obtained in these periods, they are further subdivided into 3 subgroups: those periods with bracketing plasma levels differing by less than 1 mg%, those with levels falling 1 to 3.5 mg%, and those rising 1 to 3.5 mg%. If equilibrium had not been established one would expect an excessive urinary recovery in the periods with falling levels and a deficient recovery in those with rising levels. Eighteen periods were bracketed by levels differing by less than 1 mg% and the mean out-in ratio of these is 0.990. There were 8 periods in the falling group with a mean ratio of 0.995 and 4 in the rising group with a mean ratio of 0.970. Since, if these values represented actual differences in plasma concentration, the ratios would be 117 and 0.82 for the falling and rising groups respectively we feel that equilibrium had been established. In these selected periods, an average of 99.3 mg of mannitol was excreted for every 100 mg injected (range 87-114). This small series has a standard deviation of 6.0 with a standard error of the mean of 1.1, giving for the difference 100.0-99.3 a t value of 0.64, thus failing to establish a difference between the urinary recovery of mannitol and the amount injected.

Summary and Conclusions. 1. In 92 unselected clearance periods in 29 tests on 22 patients 100.4 mg of mannitol were recovered in the urine for every 100 mg injected.

2. In 30 periods in 16 tests on 12 patients selected on the basis of plasma equilibrium and technical adequacy 99.3 mg of mannitol were recovered for every 100 mg injected.

3. These data reveal no significant extrarenal disposal of mannitol.

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Twelve-hour Nocturnal Gastric Secretion in Uncomplicated Duodenal Ulcer Patients: Before and After Healing.

ERWIN LEVIN, JOSEPH B. KIRSNER, AND WALTER L. PALMER.

From the Albert Merrit Billings Hospital, Department of Medicine, University of Chicago Clinics.

A recent study[1,2] demonstrated that the volume, concentration, and output of acid in the nocturnal gastric secretion are usually higher in patients with duodenal ulcer than in normal healthy individuals. The patients had been admitted to the hospital because of ulcer distress. Several observers have suggested that the presence of symptoms may be a contributing factor in causing hypersecretion in duodenal ulcer patients. It

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