A COMPARISON BETWEEN TORASEMIDE AND FUROSEMIDE EFFECTS AFTER APPLICATION UPON ONE KIDNEY OR AFTER I.V. INJECTION IN THE RAT

J. GENARD, R. PENNINCKX, B. CAPEL, R. LENOIR and R. KRAMP
Service de Physiologie, Université de Mons, B-7000 Mons, Belgium

INTRODUCTION

Torasemide, 1-isopropyl-3-[(4-(3'-methyl-phenylamino)-pyridine]-3-sulfonyl]urea, is a novel diuretic belonging to a new chemical series derived from 4-anilino-3-pyridine-sulfonylurea.

In the present study, the diuretic activity of torasemide and furosemide was compared using different modes of treatment, i.e. application upon the renal capsule, upon the renal cortex following decapsulation, or after i.v. injection.

METHODS AND CALCULATIONS

Anesthetized male Wistar rats weighing between 240 and 320 g were prepared as previously described with the left kidney exposed through an abdominal incision and each ureter catheterised (1). A solution of 5 % mannitol in isotonic saline was infused in order to maintain a control urine flow rate of approximately 40 ul/min/kidney.

Test-solutions were prepared as 200 ul of isotonic saline containing either placebo (time-control rats), torasemide (from $10^{-6}$ to $10^{-2}$ M) or furosemide (from $10^{-5}$ to $5.10^{-3}$ M). Following baseline determinations of urine flow ($\dot{V}$) and ion ($U_{Na\cdot} \dot{V}$, $U_{Cl\cdot} \dot{V}$, $U_{K\cdot} \dot{V}$) excretion rates (control period), a test-solution was either applied upon the left renal capsule (A.L.R.C.), i.v. injected (I.V.) or applied upon the left decapsulated kidney (D). Urine was then rapidly and serially collected from the left and the right kidney (experimental period).

Net effects of the diuretics were calculated separately for the left and the right kidney by subtracting the effects due to the mannitol infusion as well as the average of baseline measurements from urine flow and electrolyte excretion rates determined in each urine sample collected during the experimental period. The results are presented as peak and
cumulated (15, 30 and 60 min after start of treatment) effects. Statistical significance was evaluated by variance and Student paired and unpaired t-tests, as appropriate.

RESULTS

General.

Experiments were satisfactorily carried out in 97 rats. No marked differences in baseline determinations of $V$, $U_{Na}\cdot V$, $U_{Cl}\cdot V$ and $U_{K}\cdot V$ were found between the different animal groups. In 8 time-control experiments, $V$ did change little from baseline measurements during the time course of experimentation. To the converse, as expected, $U_{Na}\cdot V$ and $U_{Cl}\cdot V$ progressively increased whereas $U_{K}\cdot V$ decreased.

Torasemide and furosemide treatment

Overall effects. Statistical significant changes from time-control experiments were found after left renal capsular applications of $10^{-3}$ M torasemide and $5.10^{-4}$ M furosemide and after i.v. injections of $10^{-4}$ M torasemide and $10^{-4}$ M furosemide. The effect of torasemide (~ 60 min) was somewhat longer than the effect of furosemide (~ 40 min). The peak diuretic response occurred sooner with furosemide treatment (~ 6 min) than with torasemide treatment (~ 12 min).

Peak effects and cumulated outputs. Peak effects (highest excretion rates in a timed urine collection) and cumulated outputs (15, 30 and 60 min after start of treatment) from the left and the right kidneys were calculated. Table 1 presents a comparison of diuretic potency for salient results upon diuresis and sodium excretion from the left kidney. Results from the right kidney were almost similar.

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<td>$V$</td>
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No marked differences between left and right kidneys were found. $T$ = torasemide; $F$ = furosemide.