EFFECT OF FUROSEMIDE ON THE LOOP OF HENLE BY USING 0.45% NaCl LOADING

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Introduction

Chronic furosemide intake is thought to be a clinical model of classic Bartter's syndrome through affecting the loop of Henle in nephrons. To examine the function of the loop of Henle, the free water clearance by water loading is the standard method. However, this method is based on some assumptions and it remains to be evaluated whether this methodology correctly assesses the function of the loop of Henle. We evaluated how precisely the free water clearance method reflected the loop of Henle function by using 0.45% NaCl loading and furosemide, which exerts its pharmacological effects on electrolyte transports at the loop of Henle.

Materials and Methods

Seventeen healthy subjects (mean age, 38±8 years old; men/women, 10/7), who showed estimated glomerular filtration rate (GFR)>60 mL/min/1.73 m,^{2} were participated in the study. Informed consent was obtained from each subject. After 500 mL water intake, all subjects underwent intravenous 0.45 % NaCl infusion. Fractional distal chloride delivery [FDClD, (free water clearance + chloride clearance)/ (100 ml GFR)] as an indicator of fluid delivery to the distal nephron, and fractional distal chloride reabsorption [FDClR, (free water clearance)/(free water clearance + chloride clearance)] as an indicator of loop of Henle function were measured. Fractional excretion (FE) of electrolytes calculated by the formula of (urinary electrolyte concentrations) X (serum creatinine concentrations)/ (serum electrolyte concentrations) X (urinary creatinine concentration) were compared to assess proximal and distal tubular functions separately by using 0.45% NaCl loading. We also performed the same test in the oral pretreatment of 40 mg furosemide.

Fig 1. FDClR vs. FE-sodium

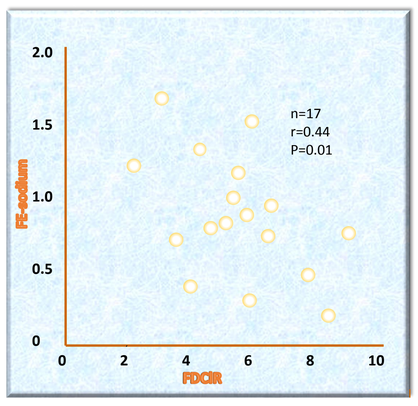


Fig 2. FDClR vs. FE-potassium

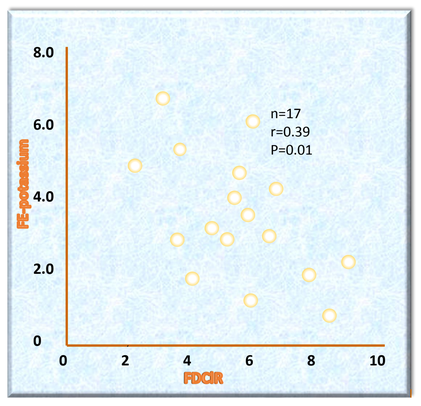


Fig 3. FDClR vs. FE-chloride

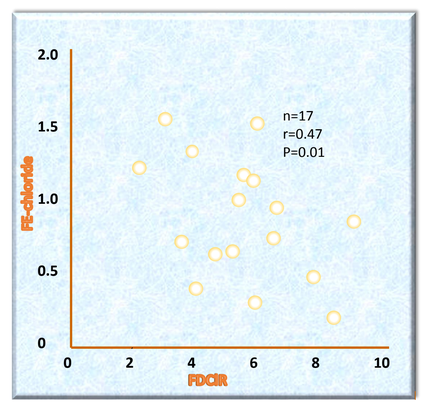


Fig 4. FDClR vs. FE-calcium

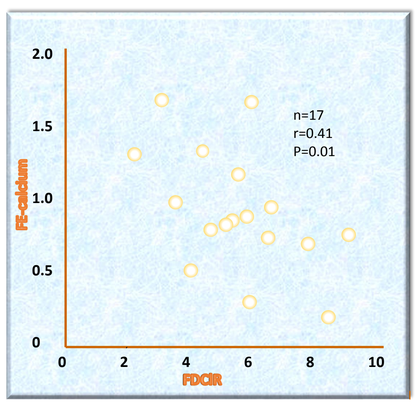


Fig 5. FDClR vs. FE-magnesium

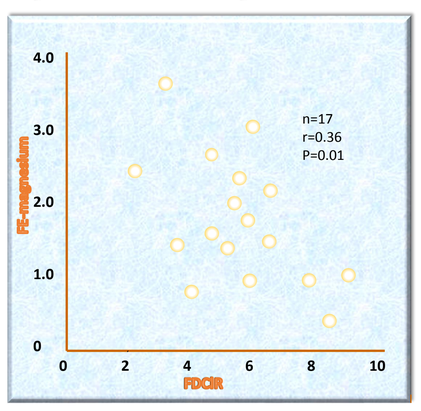


Fig 6. FDClR vs. FE-uric acid

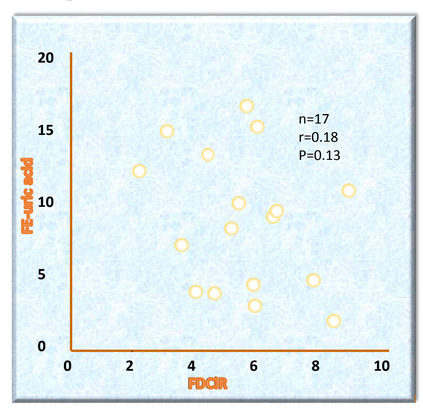
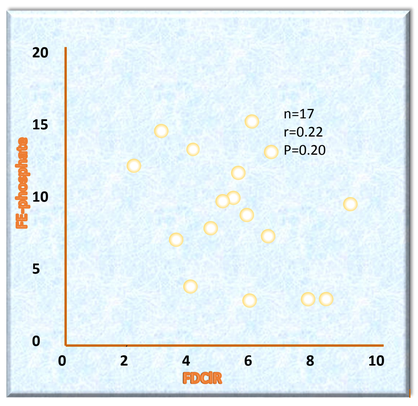


Fig 7. FDClR vs. FE-phosphate



Results

FDClR was inversely correlated (p<0.01) with markers of the loop of Henle including FE-sodium (r=0.44, Fig. 1), FE-potassium (r=0.39, Fig. 2), FE-chloride (r=0.47, Fig. 3), FE-calcium (r=0.41, Fig. 4), and FE-magnesium (r=0.36, Fig 5), but not (p>0.05) with markers of proximal tubules such as FE-uric acid (r=0.18, Fig. 6) and FE-phosphate (r=0.22, Fig. 7). Furosemide significantly decreased (P=0.03) FDClR from 82.8 ± 5.6 to 27.8 ± 11.5, and increased (P<0.05, Fig. 8) FDClD from 5.2 ± 1.3 to 16.1 ± 4.6 (Fig. 9), FE-sodium from 0.6 ± 0.3 to 7.8 ± 1.2 (Fig. 10), FE-potassium from 8.3 ± 2.9 to 27.6 ± 8.3 (Fig. 11), FE-chloride from 0.9 ± 0.2 to 11.3 ± 1.9 (Fig. 12), FE-calcium from 0.3 ± 0.2 to 5.5 ± 1.5 (Fig. 13), and FE-magnesium from 1.7 ± 0.8 to 12.1 ± 4.3 (Fig. 14). However, furosemide did not significantly change (P>0.05) FE-uric acid between 6.4 ± 1.5 and 7.9 ± 3.6 (Fig. 15) and FE-phosphate between 10.6 ± 5.6 and 13.5 ± 10.3 (Fig. 16).

Fig 8. Furosemide effect on FDClR

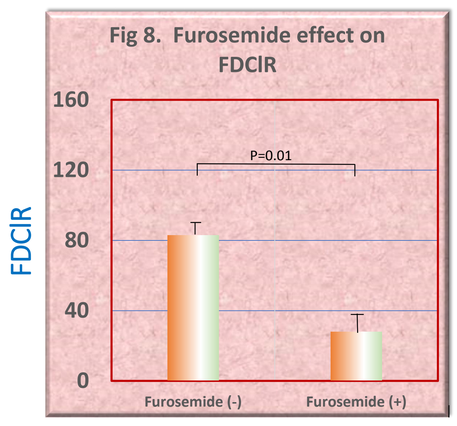


Fig 9. Furosemide effect on FDClD

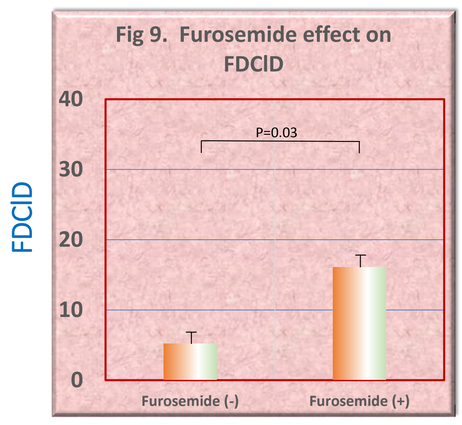


Fig 10. Furosemide effect on FE-sodium

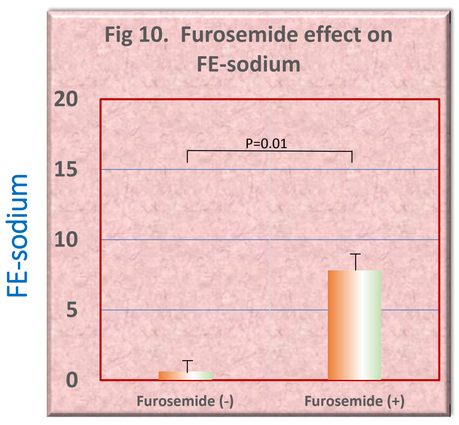


Fig 11. Furosemide effect on FE-potassium

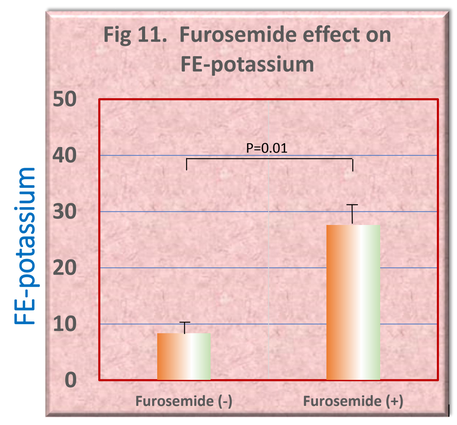


Fig 12. Furosemide effect on FE-chloride

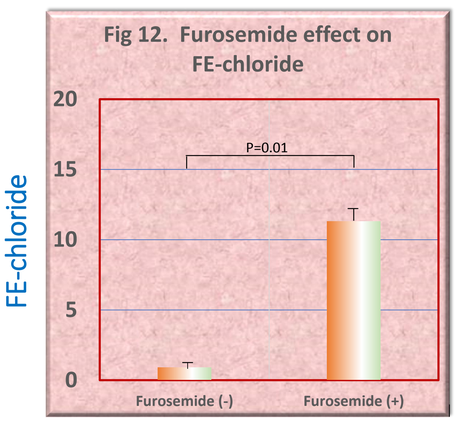


Fig 13. Furosemide effect on FE-calcium

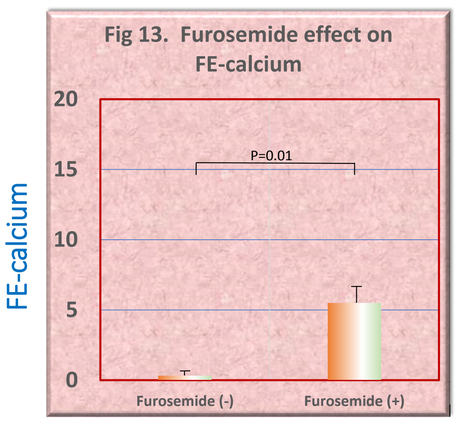


Fig 14. Furosemide effect on FE-magnesium

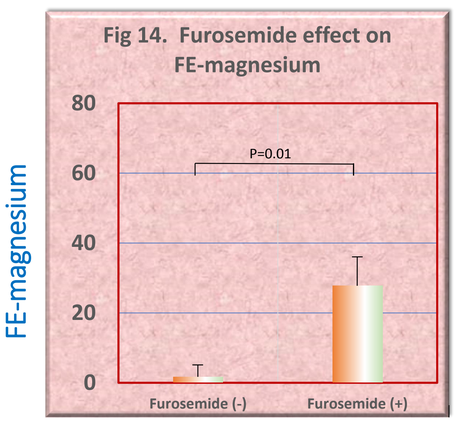


Fig 15. Furosemide effect on FE-uric acid

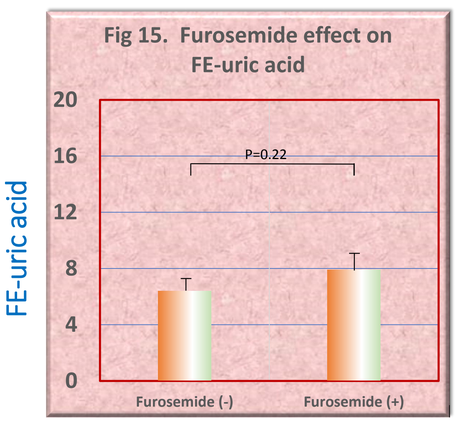
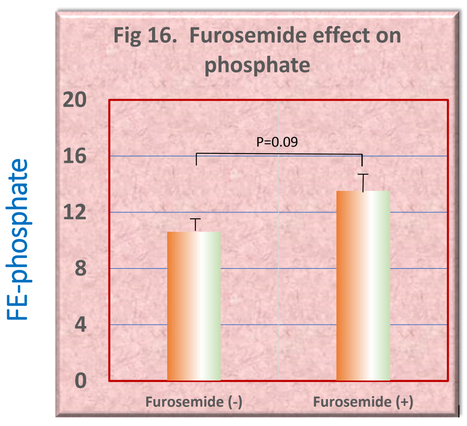


Fig 16. Furosemide effect on phosphate



Conclusions

Furosemide changed not only FDClR but also FDClD, indicating that furosemide exclusively affects the loop of Henle through its pharmacological effects. This indicates that free water clearance method using 0.45% NaCl loading well reflected the function of the loop of Henle.

54 ERA
72--MP
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DOI: 10.3252/pso.eu.54ERA.2017
ePosters supported by F. Hoffmann- La Roche Ltd.