

A MICROPUNCTURE STUDY OF THE EFFECT OF SACCHARIN INFUSION ON RENAL GLUCOSE TRANSPORT IN RATS

INTRODUCTION: During the last decades, artificial sweeteners have been extensively used because both consumers and food manufacturing companies have become interested in replacing table sugar in foods. These sweeteners are non-nutritive because they do not provide any calories. People suffering from a metabolic disease (obesity and/or diabetes) consume these substances instead of table sugar so as to control their dietary intake of carbohydrates, lower blood glucose levels and also to control their body weight. However, even though evidence of a clear relationship linking artificial sweetener use to weight gain and other metabolic health effects is limited, recent animal studies provide intriguing information that supports an active metabolic role of artificial sweeteners in the small intestine. It has been shown that this stimulation occurs by an increase in apical GLUT2 correlated with reciprocal regulation of sweet taste receptor heterodimer (T1R2/3). Preliminary data obtained in our laboratory have shown that the sweet taste receptor heterodimer (T1R2/3) is expressed in proximal tubule cells and that saccharin increases brush border membrane (BBM) levels of this protein. However, it is unclear whether saccharin can stimulate renal glucose absorption. The aim of this ongoing study is to assess the effect of a saccharin infusion on renal glucose transport.

METHODS: Free-flow micropuncture collections, from middle proximal convoluted tubules to late distal tubules in anaesthetized rats is used to assess directly the effect of saccharin on glucose reabsorption along the nephron. Wistar rats are intravenously infused with normal saline (0.9 % at 4 ml/h) containing, or not, saccharin (5 mM).

RESULTS: Our preliminary data show that, along the nephron, the tubular fluid flow rates as well as the SNGFRs do not seem to be affected by the infusion of saccharin. Conversely, glucose reabsorption seems to be altered by the presence of saccharin. The results suggest a downward trend in glucose transport in both middle (86.7 ± 2.9 and 79.9 ± 4.4 %) and late proximal tubules (85.4 ± 3.4 and 74.8 ± 6.7 %) compared with control rats. Surprisingly no significant difference is observed in glucose absorption at distal tubule sites between the two groups of rats (92.4 ± 2.0 and 88.7 ± 2.8 %; 94.7 ± 1.6 and 92.9 ± 1.7 %), indicating a compensatory mechanism occurring between the late proximal and distal tubule. Furthermore, preliminary data show that taste receptor stimulation by saccharin increases expression of SGLT1, but not SGLT2 or GLUT2 at the renal BBM.

CONCLUSION: Our findings suggest an inhibitory effect of saccharin on renal proximal glucose transport that is compensated by adaptation at a more distal site. In the kidney, glucose moves across the apical membrane by both SGLT- and GLUT-mediated processes. SGLT2 is the predominant transporter normally responsible for sodium-dependent uptake in the early proximal tubule. SGLT1 is present in the late proximal tubule and acts as a scavenger for unabsorbed glucose. Since it has been shown that gene mutations in SGLT2, and SGLT2 antagonism by blockers, lead to isolated glycosuria, we hypothesise that the decrease in glucose absorption observed during saccharin infusion is due to a reduction in SGLT2-mediated transport; moreover, increased SGLT1 expression during saccharin infusion may explain the compensatory mechanism observed between the late proximal and distal tubule.