MO626  EFFECTS OF RAMIPRIL IN LUNG AND KIDNEY ANGIOTENSIN CONVERTING ENZYME 2 (ACE2) EXPRESSION IN A TYPE 2 DIABETIC MURINE MODEL: LESSONS FOR COVID-19 INFECTION

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BACKGROUND AND AIMS: Angiotensin converting enzyme 2 (ACE2) is one of the components of the renin-angiotensin system (RAS) that mainly degrades angiotensin II to angiotensin-(1-7). ACE2 is predominantly expressed in the kidney and the heart, but it has been evidenced in type 2 alveolar lung cells, where it acts as a receptor for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In this context, a controversy arose as to whether the use of RAS blockers could increase ACE2 lung expression and the risk infection by COVID-19. This study aimed to investigate the effect of an ACE inhibitor (Ramipril) on ACE2 expression in experimental diabetes.

METHOD: 12 weeks old diabetic db/db mice (n=7) were given ramipril (8 mg/Kg/day) during 8 weeks or the respective vehicle. db/m (n=7) vehicle-treated non-diabetic mice were included as controls. ACE2 mRNA expression and enzymatic activity were studied in kidney, heart and lung samples of these animals to identify if the diabetic condition or treatment with ramipril modulated ACE2 expression.

RESULTS: In vehicle-treated diabetic db/db animals, ACE2 mRNA expression was significantly increased in the kidney (p<0.001) and ramipril treatment reversed this effect (p<0.026). In the heart, ACE2 expression decreased in db/db when compared to db/m littermates (p=0.035) and ramipril had no effect. We found no differences in ACE2 gene expression in the lung. Besides, ACE2 enzymatic activity was increased in the kidney (29%) and also in the lung (16%) of db/db mice when compared to controls. Ramipril treatment decreased ACE2 activity a 19% in the lung and had no effect in the kidney when compared to untreated db/db (see figure). In the heart, ACE2 activity tended to decrease in db/db mice (29%) when compared to db/m and ramipril increased ACE2 activity (18%) but did not exceed the cardiac ACE2 activity of the db/m.

CONCLUSION: ACE2 is increased in the kidney and the lung, and decreased in the heart of diabetic mice. Ramipril treatment restores ACE2 levels. The results suggest that ACE inhibitors do not increase ACE2 expression and the activity decrease exerted in the lung may be protective against COVID-19 infection.