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JNJ39758979 prevents the progression of diabetic nephropathy in male DBA2/J mice

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The incidence of diabetes and the related morbidity of diabetic nephropathy requires the identification of new therapeutic strategies. In the last decades, new and growing evidence on the possible role of histamine in diabetes have been provided. In particular, the histamine receptor H4R is emerging as a new promising pharmacological target for diabetic nephropathy. The aim of this study was to evaluate the efficacy of H4R antagonism by JNJ39758979 on the prevention of diabetic nephropathy progression in a murine model of diabetes induced by streptozotocin injection. JNJ39758979 (25, 50, 100 mg/kg/day p.o.) was administered for 15 weeks starting from the onset of diabetes. JNJ39758979 did not significantly affect glycaemic status or body weight. The urine analysis indicated a dose-dependent inhibitory effect of JNJ39758979 on albumin-creatinine-ratio, the creatinine clearance, the 24 h urine volume and pH urine acidification ($P<0.05$). The beneficial effects of JNJ39758979 on renal function paralleled comparable effect on renal morphological integrity. These effects were sustained by a significant infiltration and fibrosis reduction. Notably, megalin and sodium-hydrogen-exchanger 3 expression was preserved. Our data suggest that H4R participate to diabetic nephropathy progression through both a direct effect on tubular reabsorption and an indirect action on renal tissue architecture via inflammatory cells recruitment. Therefore, H4R antagonism emerges as a possible therapeutic approach to counteract diabetic nephropathy development.

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