THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

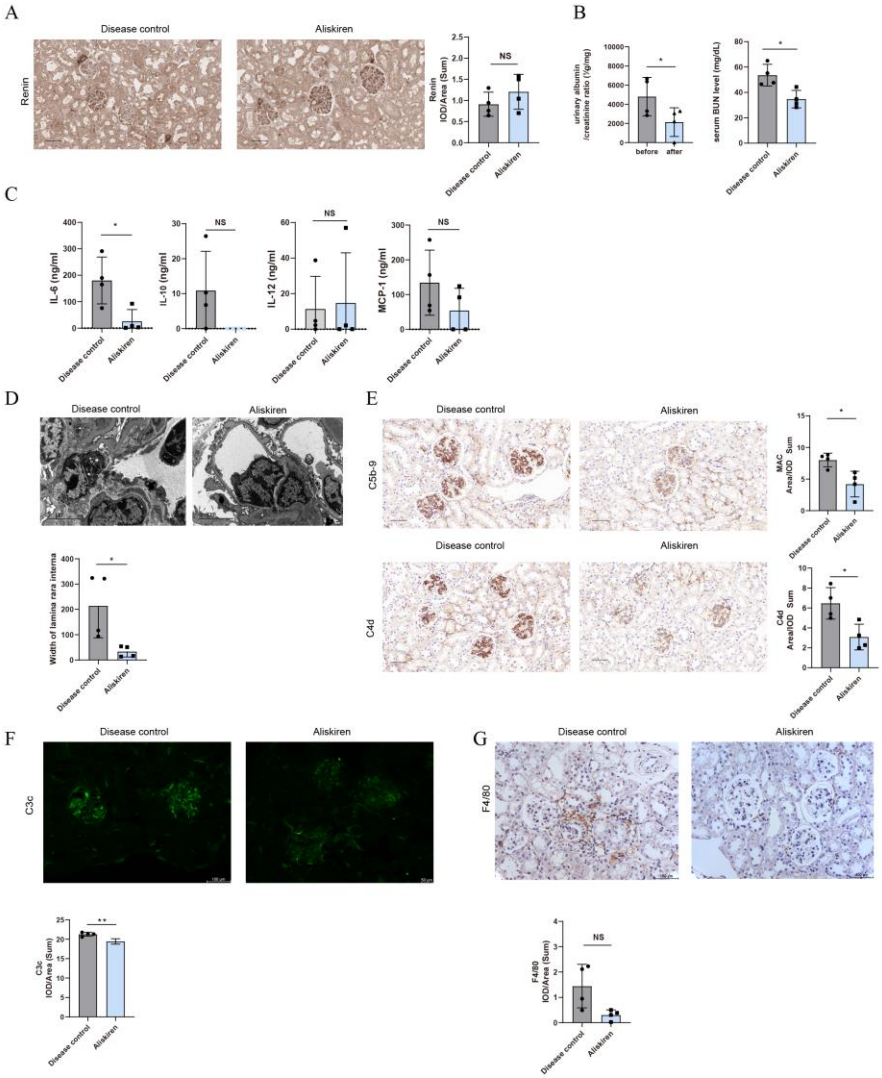
Abstract Submission No.: A-1107

Aliskiren: A Promising Intervention for Reducing Complement Deposition in Postpartum Atypical Hemolytic Uremic Syndrome

Chuqiao Wang, Yifang Hu, Feifei Chen, Ying Tan, Minghui Zhao
Department of Internal Medicine-Nephrology, Peking university first hospital, China

Objectives : Atypical hemolytic uremic syndrome (aHUS) is a rare complement-mediated disease leading to thrombotic microangiopathy (TMA). Pregnancy-associated aHUS refers to aHUS occurring during or after pregnancy. Renin inhibitors have shown potential therapeutic effects on complement-mediated diseases. In our study, we aimed to investigate the therapeutic implications of renin inhibition, specifically with aliskiren, in postpartum aHUS.
Methods : The W1206R mutant mice ($FH^{R/R}$)created by laboratory of Wen-chao Song developed the phenotype of TMA. Based on this model, our team created postpartum aHUS mice. Female wildtype ($FH^{W/W}$) mice were mated with male heterozygous Cfh mutation ($FH^{W/R}$) mice to obtain offspring female $FH^{W/R}$ mice which did not result in disease phenotype. After multiple pregnancies, these offspring mice developed manifestations of renal TMA gradually. Then postpartum $FH^{W/R}$ mice were divided into two groups: a control group receiving vehicle and a treatment group receiving aliskiren at a dose of 30 mg/kg/day for 8 weeks. Immunofluorescence, immunohistochemistry, and electron microscopy were used to evaluate the effects of aliskiren on postpartum aHUS.
Results : Immunohistochemical staining revealed renin deposition in the kidneys of aliskiren-treated mice and controls. Aliskiren treatment resulted in decreased urine albumin/creatinine and blood urea nitrogen levels compared to the disease control group. Additionally, aliskiren significantly reduced IL-6 levels in kidney tissues. Electron microscopy showed alleviation of subendothelial expansion, and immunostaining demonstrated reduced complement deposition in the kidneys of aliskiren-treated mice. Furthermore, there was a trend towards decreased macrophage infiltration after treatment.
Conclusions : In conclusion, our study suggests that aliskiren has promising protective effects in postpartum aHUS mice. Aliskiren treatment ameliorated complement composition improved kidney function, and reduced inflammation in ameliorated aHUS mice. These findings highlight the therapeutic potential of renin inhibition, specifically with aliskiren, in postpartum aHUS.

figure3-03.png


A
Disease control
Aliskiren
Renin
Renin IOD/Area (Sum)
NS
B
urinary albumin /creatinine ratio (㎎/g)
before
after
serum BUN level (mg/dL)
C
IL-6 (ng/ml)
IL-18 (ng/ml)
IL-12 (ng/ml)
MCP-1 (ng/ml)
D
Width of lamina rara interna
E
C5b-9
MAC Area/IOD Sum
C4d
C4d Area/IOD Sum
F
C3c
C3c IOD/Area (Sum)
G
F4/80
F4/80 IOD/Area (Sum)