Moxifloxacin exacerbate aortic aneurysm and aortic dissection by increasing osteopontin protein expressions

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Backgrounds: Aortic aneurysm and dissection (AAD) are fatal diseases that are caused by the rapid destruction of the aortic wall. Osteopontin (OPN), an inflammatory extracellular matrix protein, is involved in the formation and development of AAD. Fluoroquinolones are among the most widely used antibiotics. On the other hands, recent clinical studies indicated an association between fluoroquinolone use and increased risk of AAD. However, this mechanism remains obscure. In this study, we examined the effects of moxifloxacin (MFLX), one of the fluoroquinolones, on the development of AAD in model mice and investigated OPN expressions in aortic tissues from AAD-model mice and in macrophages (RAW264.7 cell).

Methods and results: C57BL/6J mice (4weeks of age) were fed a high-fat diet. Four weeks later (8weeks of age), the mice were infused with vehicle or angiotensin II (1000 ng/min/day) via osmotic minipumps for 4 weeks. MFLX (30 and 100 mg/kg/day) or water (vehicle) was orally administered to these mice for last 3 weeks. MFLX (100mg/kg/day) caused to development of AAD in model mice. Additionally, OPN protein expressions were increased in aortic tissues from MFLX-treated mice compared with from vehicle-treated mice. Next, to examine the effects of MFLX on OPN expression in macrophages, RAW264.7 cells were treated with various concentration of MLFX for 24 h. MFLX dose-dependently increased OPN protein expressions in RAW264.7 cells; these increases reached at peak at 300 mM MFLX. In addition, OPN expressions in 300 mM MFLX-treated RAW264.7 cells were time-dependently increased and peaked at 24h.

Conclusion: MFLX increased OPN protein expressions in aortic tissues from moderate-AAD model mice and in macrophages. Therefore, MFLX may induce the onset of AAD by increasing expression of OPN.