PLEIOTROPIC BENEFITS OF METFORMIN IN ATTENUATION OF ATHEROSCLEROSIS AND VASCULAR AGING

Moderated Poster Contributions
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Background: Several population-based studies have shown that even at similar glycemic level compared with other medications for DM2, metformin attenuates all cause mortality and MI. However, there is a paucity of data on cardiovascular benefits of metformin.

Methods: Using ApoE-/- C57BL/6J mice, we tested whether metformin attenuates atherosclerosis and/or vascular aging in response to high fat diet (HFD) or angiotensin II (Ang II) treatment delivered by using osmotic minipumps.

Results: At one month, the mice in HFD+metformin group compared to those in HFD+saline group, had less atherosclerotic plaques as well as attenuated vascular aging (Figure-1). In Ang II study set, we found that vascular aging-induced by Ang II was almost completely abolished by metformin. This was accompanied by modulation in hypertension-induction effect of Ang II. Moreover, we found that angiotensin II type 1 receptor (AT1R) up-regulation in the aortas of mice fed HFD was significantly modulated by metformin suggesting AT1R disruption as a mechanism for vascular benefits of metformin. Furthermore, the vasculoprotective benefits of metformin in these study sets were accompanied by modest but significant weight loss. In HFD study sets, metformin use also led to significant decrease in the serum levels of several inflammatory cytokines including IL-1α, MCP-1, M-CSF, and TIMP-1.

Conclusions: In this study we found that metformin provides pleiotropic benefits leading to the amelioration of both atherosclerosis and vascular aging.