ISGE
GYNECOLOGICAL ENDOCRINOLOGY
THE 18TH WORLD CONGRESS
7-10 MARCH 2018 FLORENCE, ITALY

Gonadotrophins and cardiovascular disease

X Fu (CN) [1]

Postmenopausal atherosclerosis (AS) has for decades been attributed to estrogen deficiency. Although the follicular stimulating hormone (FSH) levels rise sharply in parallel, the direct effect of FSH on AS has never been investigated. In this study, we explored the possible role of FSH in the development of AS. In ApoE knockout mice, administration of FSH increased the atherosclerotic lesions and serum VCAM-1 concentration. Importantly, in blood samples of postmenopausal women, we detected significantly higher levels of FSH and vascular cell adhesion molecule-1 (VCAM-1) compared with those from premenopausal women, and there was a positive correlation between these two molecules. In cultured human umbilical vein endothelial cells (HUVECs), FSH receptor (FSHR) mRNA and protein expression were detected and FSH enhanced VCAM-1 expression. This effect was mediated by the activation of nuclear factor ?B (NF-?B), which was sequentially enhanced by the activation of PI3K/Akt/mTOR cascade. FSH first enhanced G?S activity resulting in elevated cAMP level and PKA activity, which relayed the signals from FSHR to the PI3K/Akt/mTOR cascade. Furthermore, FSHR was detected in endothelial caveolae fraction and interacted with caveolin-1 and G?S. The disruption of caveolae or the silencing of caveolin-1 blocked FSH effects on signaling activation and VCAM-1 expression, suggesting the existence of a functional signaling module in membrane caveolae. Finally, FSH increased human monocyte adhesion to HUVECs which was reversed by the VCAM-1 neutralizing antibody. Taken together, our work demonstrated, for the first time, that FSHR was located in the membrane caveolae of HUVECs and FSH promoted VCAM-1 expression via FSHR/G?S /cAMP/PKA and PI3K/Akt/mTOR/NF-?B pathway. This may contribute to the deleterious role of FSH in the development of AS in postmenopausal women.

[1] Guangzhou Medical University, Guangzhou