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DIABETES AND ESTROGENIC CONTROL OF INDUCIBLE NITRIC OXIDE SYNTHASE IN RAT AORTIC SMOOTH MUSCLE CELLS

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We previously reported that 17ß-estradiol (E_2) reduces cytokine-mediated inducible NO synthase (iNOS) activity in rat aortic smooth muscle cells (SMC) [1].
As a follow-up of the above study, the effects of estrogen on iNOS function were determined in SMC isolated from the aorta of streptozotocin-diabetic rats. After incubation with a cytokine mixture for 24 h, iNOS protein levels were lower in diabetic than in control SMC as determined by Western blot. This was associated with lower iNOS mRNA expression and enzyme activity in diabetic SMC, as determined by nitrite accumulation in the culture medium. Treatment with 10^{-11}–10^{-9} M E_2 for 24 h dose-dependently reduced iNOS protein levels in control, but not in diabetic SMC. On E_2 treatment, iNOS mRNA expression was reduced in control, but rose in diabetic SMC. A similar pattern was observed for the amount of nitrite in the medium. Cytokine treatment for 24 h consistently reduced estrogen receptor (ER) α and ß mRNA expression in both SMC groups. However, ERα and ERß mRNA levels were greater in diabetic than in control SMC.
In conclusion, iNOS activation is delayed and insensitive to estrogen in diabetic SMC, which in turn express larger amounts of ER genes compared with non-diabetic SMC. This mechanism may be involved in the loss of cardiovascular protection seen in diabetic *versus* non-diabetic females.

References

1. Zancan V, Santagati S, Bolego C, Vegeto E, Maggi A, Puglisi L. 17ß-estradiol decreases nitric oxide synthase II synthesis in vascular smooth muscle cells. *Endocrinology* 1999;140:2004-2009.