Farmacologia Cardiovascolare dei Donatori di Ossido d'Azoto (NO): Prospettive Terapeutiche
6° Convegno Monotematico SIF – Milano, 31 Maggio 2002

ANTIOXIDANT TREATMENT AFFECTS VASCULAR RESPONSES IN THE AORTA OF SHORT-TERM DIABETIC RATS

C. Pinna, L. Puglisi
Department of Pharmacological Sciences, via Balzaretti 9, 20133 Milan (Italy)

Diabetes mellitus is associated with gender-specific vascular complications due to increased oxidant stress (1). To determine the effects of a low dose of antioxidant drugs on vascular function in short-term diabetes, we treated rats with 2 unrelated drugs sharing antioxidant properties, lercanidipine and Leucoselect™ (Indena SpA -Italy) both 3 mg/Kg/day for 1 wk after diabetes induction. Rats were injected with either streptozotocin (60 mg/Kg i.v.) or the vehicle, and were divided into 4 groups of both genders: non-diabetics, untreated diabetics, lercanidipine- and leucoselect-treated diabetics. Aortic preparations were mounted in organ baths for isometric tension recording.
Maximal NO-mediated relaxations (% norepinephrine contraction) to L-nitroarginine methylester (L-NAME: 130 ± 3.9 vs 118 ± 3.9), superoxide dismutase (SOD: 71 ± 6.0 vs 57 ± 7.3) and acetylcholine (ACh: 92 ± 4.0 vs 84 ± 6.0) were significantly greater in female compared with male non-diabetic rats. Diabetes increased contractility (mN/mg) to norepinephrine (NE: 2.30 ± 0.30 vs 1.36 ± 0.20 and 2.30 ± 0.35 vs 1.60 ± 0.30) and L-NAME (155 ± 10 vs 130 ± 3.9 and 158 ± 13 vs 118 ± 3.9) in females and males, whereas relaxation to ACh and the prostacyclin analogue iloprost were significantly attenuated in females only. Lercanidipine and Leucoselect restored, in part, responses to NE, ACh and iloprost without affecting those to L-NAME and the exogenous NO donor sodium nitroprusside.
These results suggest that female rat aorta is more exposed to diabetic vascular injury, as shown by impaired NO-mediated relaxations. Antioxidant treatment prevents most alterations of aortic reactivity in diabetic females. Therefore, antioxidants display gender-specific vascular protective effects in short-term diabetes.

References

1. Fedele D., Giuliano D. (1997). *Drugs* 54, 414-421.