EFFECT OF A NITRIC OXIDE-RELEASING ASPIRIN DERIVATIVE, NCX 4016, ON ENDOTHELIAL DYSFUNCTION OCCURRING IN DIABETIC RATS: A BIOCHEMICAL AND MORPHOLOGICAL STUDY

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Vascular endothelium has a pivotal function in the regulation of hemodynamics, blood fluidity and blood vessels patency [1]. These properties mostly depend on products resulting from endothelial nitric oxide synthase activity and cyclooxygenase pathway[2, 3]. Several diseases including diabetes mellitus are associated with a functional and/or structural endothelial impairment. As a result, diabetic patients have elevated risk of vascular complications[4]. In this study we examined the effect of both NCX 4016, a nitric oxide (NO) releasing aspirin derivative, and aspirin (ASA) treatment on the aortic endothelium of diabetic rats by using scanning and transmission electron microscopy (SEM and TEM, respectively).

Methods. The study was conducted in young adult male Wistar rats (n= 78, 165-190 g; Harlan Italy). Diabetes was induced by streptozotocin (65 mg/kg i.p.). One week after injection, diabetic rats (glucose 200-600 mg/dl) were randomly divided into 4 groups: NCX4016 100 mg/kg (n=12), ASA 54 mg/kg (n=12), Vehicle (n=12) and diabetic controls (DC, n=12). Non-diabetic (ND) controls were studied along with the diabetic rats. The drugs were given daily for 6 weeks by the oral administration. Metabolic control was assessed by measuring blood and urine metabolites, and 24-h urine volume. Immediately after sacrifice, the thoracic aorta was removed and quickly processed for SEM and TEM study.

Results. STZ treatment induced a persistent increase in blood glucose which was not influenced by pharmacological treatments. Values of blood metabolites were in line with the diabetic status. Interestingly, the BUN values increased in DC, Vehicle and ASA groups whereas they were normal in NCX4016 rats. SEM study of aortic endothelium showed: i) many and widespread pathological signs in DC, Vehicle and ASA groups; ii) scanty and scattered pathological findings in ND and NCX4016 rats. TEM study of aortic endothelium confirmed the results obtained by SEM.

Our data document the protective effects of NCX 4016 on macrovascular endothelium of diabetic rats and, possibly, on kidney function. In fact, NCX 4016 protected endothelial structure and did not change blood urea values. Since ASA had no protective action, possibly NCX 4016 exerted its beneficial action by releasing NO.

References

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