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Short communication

K^+-INDUCED RELAXATION IN VASCULAR SMOOTH MUSCLE OF ALLOXAN-INDUCED DIABETIC RATS

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The effects of different concentration of intracellular potassium (K^+), on rate of relaxation were studied in isolated aortae of normal and diabetic rats. The relaxation responses induced by raised extracellular potassium concentration was attenuated in aortic rings from diabetic rats. Possible reasons are discussed in the text.

Keywords: Smooth muscle, alloxan, diabetes, K^+

It has been known for many years that the potassium ion is a vascular dilator in vivo. Intra arterial injection of potassium had been reported to cause vasodilation, which was shown to be a direct effect on the vascular smooth muscle cell since the response still, occurred after denervation or adrenergic blockage (Donald, 1176).

The activity of Na, K-Atpase, an enzyme known to play a role in the membrane Na-K Pump of most cells, has been shown to be, in part, dependent on potassium concentration (Skon, 1965). It is now generally accepted that increasing extracellular potassium or intracellular sodium ion concentrations stimulates the pump while decreasing these ion concentration inhibits the pump.

Vascular complications are commoner in the diabetic than in non-diabetic populations (Altura et al, 1979). However, the nature of the process that results to these complications is not yet clear.

The dilating action of K^+ on diabetes vessels have received very little attention. The present study examines the influence of (K^+) on contractile responses of alloxan – induced diabetic rat aortae.

MATERIALS AND METHODS

Male Wistar rats initially weighing 120 – 140gm and aged 10-12 weeks were used for study. They are randomly divided into control and diabetic groups. Each test animal was made diabetic by intraperitoneal injection of a alloxan (40mg/kg body weight) in citrate buffer.

All animals had free access to food and water and were monitored daily for the development of glycosuria by testing for the presence of reducing sugar in the urine. Diabetes was confirmed when blood glucose (obtained by cutting the tip of the tail) was 4 times in excess of the normal. Two weeks after induction of diabetes, rats were killed by stunning and their aortae quickly isolated, freed of adhering connective tissue with microdissecting forceps before it was removed and placed in a petri dish cotaining normal PSS. Blood was gently flushed out of the lumen of the aorta with a 1ml syringe attached to a 23 guage needle and containing normal PSS.

The aorta was cut into approximately 2mm ring segment and suspended between L-shaped fine stainless steel rod and a stainless steel hook. This was transferred into a 20ml jacketed organ bath containing normal PSS of the following composition (MM/L):
Nacl, 119.0; Kcl, 4.7; KH_2PO_4, 1.2; $MgSo_{44}$ 1.2; Cacl, 1.6; $NaHCO_3$, 1.25gm, Glucose, 2.0gm and PH 7.4. The solution was continuously oxygenated with 90% 0_2 and 5% Co_2 gas mixture and maintained at 37°C. The hook was anchored to the base of the organ bath and the stainless steel rod was connected to an isometric force displacement transducer (FT.03), which was coupled to a grass model 79D polygraph for recording tension. The tissue was allowed to equilibrate for 90 minutes under a resting tension of 1.5 g prior to the commencement of experiments.

At the end of equilibration period the rings were exposed to K^+ free 1.6 Mol $^{-1}$-1 Ca^{2+} PSS for 30 minutes before being stimulated with 10^{-7} mol. 1^{-1} NA. When the contraction was stable, K^+ was added to the bath cumulatively, resulting in concentration dependent relaxation. The magnitude of relaxation was expressed as a percentage of the initial contractile response to NA in K^+- free PSS. K^+-free PSS was prepared by substituting KCL (and KH_2PO_4) in the PSS with equimolar concentrations of Nacl (and NaH_2Po_4) respectively. Values are presented as mean + SEM.

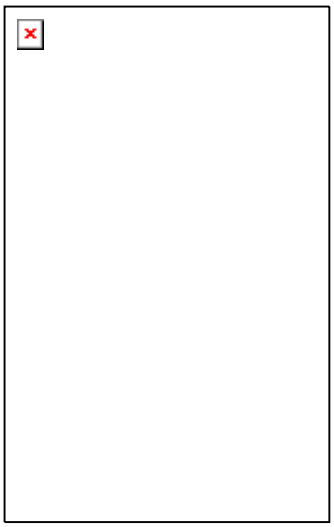

Figure 1.
A representative tracing that illustrates K^+- induced relaxation of a rat aortic strip pre-contracted by noradrenaline (NA)

RESULTS

Diabetic rats had elevated blood glucose level when compared with age-matched controls. Additionally, they exhibited other symptoms commonly associated with diabetes mellitus (e.g polyuria, polydipsia and diarrhoea).

Figure 1 is a representative tracing of the protocol used to study K^+ - induced relaxation. In all experiments, K^+ caused concentration – dependent relaxation following precontraction by noradrenatine.

K^+- induced relaxation was significantly attenuated in rings from diabetic rats (fig. 2).

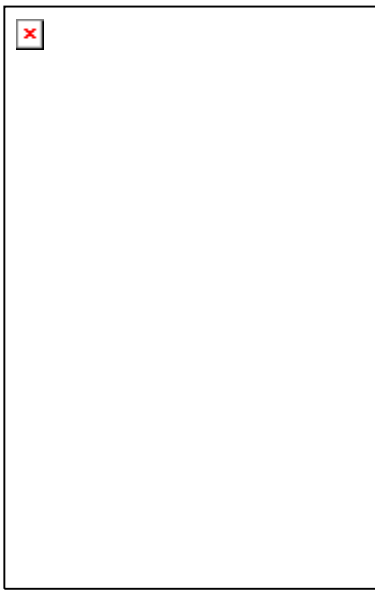

Figure 2
K^+ - induced relaxation

DISCUSSION

Result of the present study show that the relaxation responses induced by raised extracellular potassium concentration is significantly attenuated in aortic rings from diabetic rats.

The resistance of the aortic smooth muscle membrane to depolarization was investigated. This was done indirectly be assessment of Atpase activity. The result shown in figure 2 reveal that the activity of the Na^+ - K^+ pump, is decreased in the aortae of the diabetic rats.Since, the Na^+ - K^+ pump works towards maintaining the resting membrane potential (Webb and Bohr, 1978), a decrease in the activity of the Na-K Atpase and hence in the Na-K pump would tend to make the membrane more depolarizable.

The attenuated KCI-induced relaxation of aortic rings from diabetic rats observed in this study when compared to those of control can therefore be interpreted to be an indication of decrease in Na^+ - K^+ Atpase activity.

In conclusion, the present study demonstrates that the magnitude of K^+ - induced relaxation may be used as an index of the effect of specific agents or interventions (disease state as diabetes) on the activity of this important enzyme system.

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