504

Dambros M[1], de Jongh R [2], van Koeveringe G [2], van Kerrebroeck P[2], Palma P[3], Z Riccetto C[3]
1. São Francisco University, 2. Maastricht University, 3. State University of Campinas

FLAVONOID PROTECTS PIG DETRUSOR NERVES FROM ANOXIA-GLUCOPENIA INJURIES

Hypothesis / aims of study

Recent studies suggested that the urinary bladder might undergo cyclical ischemia reperfusion during overdistension or increased pressures due to outlet obstruction, which in turn may lead to oxidative stress and the injury by free radical [1]. Furthermore, the periodic bladder ischaemia during obstructed micturition has been suggested to result in the partial denervation of the detrusor smooth muscle, through ischaemic and reperfusion injury to the post-ganglionic parasympathetic neurones within the bladder wall [2]. The goal of this paper was to test the capability of the flavonoid galangin to protect pig urinary bladder from damage due to a period of anoxia/glucopenia and reperfusion.

Study design, materials and methods

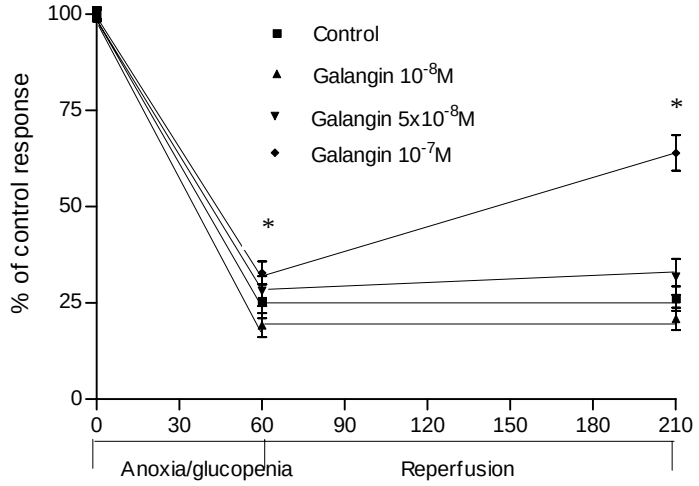
Smooth muscle strips of the pig bladder were mounted for tension recording in small organ baths. After the equilibration period, the tissue was subjected to electrical field stimulation every 15min until the response was reproducible. Then, detrusor strips were subjected to 60 min of anoxia/glucopenia followed by 150 min of reperfusion. Under ischaemic-like conditions, glucose was replaced isosmotically with NaCl, the solution was gassed with 95% N_2, 5% CO_2. Oxygen tension in the organ baths was measured using a fine platinum oxygen electrode, previously calibrated in solutions of known oxygen tension. During this 210-min period, intrinsic nerves were stimulated electrically at 60 min and 210 min. The response of the strips to electrical field stimulation was expressed as a percentage of the initial response in Krebs solution, taken to be 100%. Galangin, at different concentration, was added to the perfusion medium during the ischaemic conditions and the first 30 min of reperfusion as it is supposed that the major damage to the tissue develops not only during ischaemia, but also when the oxygen reaches again the tissue.

Results

The response to electrical field stimulation declined in the combined absence of oxygen and substrate, reaching 25% of the initial response within an hour, in Krebs solution medium. After reintroduction of normal conditions, the recovery of the response to electrical field stimulation was poor, reaching a maximum of about 26% of the initial response in 2 h.

Galangin at 10^{-7}M concentration improved significantly the electrical field stimulation-induced contractile response both in anoxia/glucopenia and in reperfusion phase, reaching 33% $\pm$ 3.02% at 60 min and 64% $\pm$ 4.1% at 210min ($p < 0.05$ compared to non-treated group). At 10^{-8} and $5x10^{-8}$M there was not any significantly effect compared to non-treated group.

Graph: Electrical field stimulation-induced contractile responses of pig detrusor strips subjected to 60 min of anoxia/glucopenia and subsequent 150 min of reperfusion. Experiments carried out in the absence or presence of galangin at different concentrations. Galangin was applied for the first 90 min of the experiment. Results are expressed as mean $\pm$ S.E.M. Significant differences from the control group are indicated; * $p < 0.05$.



Interpretation of results

Galangin at 10^{-7}M significantly improved the response of the strips to EFS both at the end of ischaemia and reperfusion. On the contrary, neither 10^{-8}M nor $5x10^{-8}$M galangin had significant effects. It is concluded that galangin can partially counteract the ischaemia-reperfusion injury in the pig urinary bladder.

Concluding message

In conclusion, galangin is a natural flavonoid exerting protective effects on bladder contractility. Although it remains to be elucidated, outlined in the present investigation, we suggest that the anti-oxidant compound, galangin, might have a possible role in treating bladder dysfunction.

References

1. Correlation of ischemia/reperfusion or partial outlet obstruction-induced spectrin proteolysis by calpain with contractile dysfunction in rabbit bladder. Urology 49:293-300, 1997.
2. Alternations in the physiological properties of urinary bladder smooth muscle by bladder emptying against an obstruction. J Urol 184:51-8, 1997.