The phosphodiesterase type 4 inhibitor, rolipram, is more efficient to relax detrusor smooth muscle in rats with overactive bladder than in control rats.

**HYPOTHESIS, AIMS OF STUDY**

- Detrusor relaxation is mainly mediated by the cAMP pathway, which is activated through stimulation of adenylyl cyclase via the fixation of noradrenaline to β-adrenoceptors.
- At the cellular level, the intensity and the duration of the intracellular cAMP and cGMP signals are partly regulated by the phosphodiesterase (PDE) enzymes whose functions are to degrade cyclic nucleotides into their inactive metabolites.
- Among the 11 distinct PDE families described, PDE4 is selective for cAMP hydrolysis, and it has been widely evidenced in overactive bladder (OAB) i.e with partial bladder outlet obstruction (BOO).

**STUDY DESIGN, MATERIALS & METHODS**

**Animal preparation**

Female Wistar rats (200-225 g) were anesthetized with isoflurane. Entire bladders were excised and placed in Krebs-HEPES buffer (with the following millimolar composition: NaCl 118.0; KCl 4.7; MgSO4 1.2; NaH2PO4 1.2; CaCl2 2.5; NaHCO3 4.2; glucose 11.1; HEPES 20.8; pH 7.4). The bladder dome was isolated from the trigone region and four longitudinal strips were then mounted isometrically in 5 ml organ baths filled with Krebs-HEPES buffer maintained at 37°C and continuously bubbled with 95%O2-5%CO2.

**Surgical procedure to perform partial BOO**

After 6 weeks of partial bladder outlet obstruction, rats were anesthetized with isoflurane. Entire bladders were excised and placed in Krebs-HEPES buffer (with the following millimolar composition: NaCl 118.0; KCl 4.7; MgSO4 1.2; NaH2PO4 1.2; CaCl2 2.5; NaHCO3 4.2; glucose 11.1; HEPES 20.8; pH 7.4). The bladder dome was isolated from the trigone region and four longitudinal strips were then mounted isometrically in 5 ml organ baths filled with Krebs-HEPES buffer maintained at 37°C and continuously bubbled with 95%O2-5%CO2.

**RESULTS**

- **Effect of rolipram on carbachol-induced contractions in detrusor smooth muscle from non-obstructed and obstructed rats**

  ![Graph showing the effect of rolipram on carbachol-induced contractions](image)

  - Rolipram is more efficient to relax carbachol-induced contractions of detrusor from obstructed rats than from non-obstructed rats.

- **Effect of rolipram on carbachol-induced contractions in detrusor smooth muscle in presence of forskolin**

  ![Graph showing the effect of forskolin on carbachol-induced contractions](image)

  - The presence of forskolin significantly enhanced the relaxing effect of rolipram both in non-obstructed and non-obstructed rat.

**CONCLUSIONS**

- The PDE4 inhibitor rolipram is more efficient in relaxing carbachol pre-contracted detrusor strips in rats with partial BOO than in control rats.
- These results suggest a change in the control of the cAMP pathway in rats with overactive bladder due to BOO.
- PDE4 inhibitors deserve further investigation for the treatment of OAB.