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EFFECT OF CYCLOOXYGENASE-2, [A PROSTAGLANDIN INHIBITOR] ON ATP-INDUCED CONTRACTION IN RAT BLADDER DETRUSR MUSCLE

Aim of Study

To study age-related changes in ATP induced contractions, we investigated the contractile responses of prostaglandin linked mechanisms in rat bladder detrusor muscle strips using two newly developed inhibitors, cyclooxygenase (COX) and prostaglandin (PG) E2.

Methods

Urinary bladders were obtained from male Wistar rats at the ages of 9 weeks [young], 24 weeks [adult], and 24 months [aged]. ATP contractions of the urinary bladder muscle strips were measured isometrically. The magnitudes of the ATP-induced phasic contraction were compared between the three age groups. During the contractions, prostanoid concentrations in the organ bath medium were measured using the enzyme immunoassay method. To clarify the PG-linked mechanism, we used suramin (non-selective P2 receptor antagonist), JTE-522 (selective COX-2 inhibitor), and ONO-8711 (selective PG E2 anatgonist) before ATP stimulation.

Results

ATP-induced phasic contraction increased with age. After ATP stimulation, a significant increase of PG E2 in the organ bath medium was observed. The inhibitory effect of P2X receptor antagonist (suramin) decreased with age. The Effects of indomethacin in aged were larger than adult. Selective COX-2 inhibitor showed no apparent inhibitory effects. PG E2 antagonist showed an inhibitory effect in young and adult.

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Magnitudes of ATP-induced contractions and effects of inhibtors (g/tension)

	young(N=6)	adult(N=8)	aged(N=4)
control	1.86±0.35	2.35±0.28	2.21±0.38
suramin	0.84±0.35 (45.1±18.3%)	1.25±0.31 (53.2±15.6%)	1.28±0.35 (57.9±15.8%)
indomethacin	-	1.68±0.28 (71.0±11.9%)	1.41±0.34 (64.1±15.4%)
PG E2 antagonist	0.94±0.28 (50.5±15.1%)	1.34±0.28 (57.2±11.9%)	1.87±0.29 (84.6±13.1%)
COX-2 inhibitor	-	2.18±0.32 (92.7±13.6%)	2.08±0.40 (94.1±18.1%)

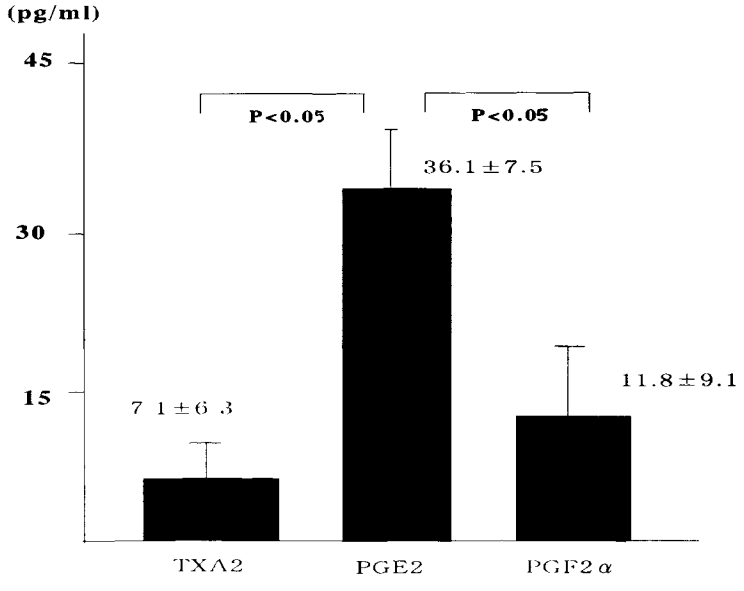
Conclusions

We observed the increase of PG E2 in the oragan bath medium after ATP stimulation[1]. In this study, PG E2 antagonist showed an inhibitory effect in young and adult. Indomethacin, a non-selective PG synthesis inhibitor, showed about a half inhibitory effect of that by extracellular P2X receptor antagonist. These findings suggested that the ATP-induced contraction is partly transmitted by the PG E2 producing process, not only the G-protein-coupled inositol triphosphate related pathway.

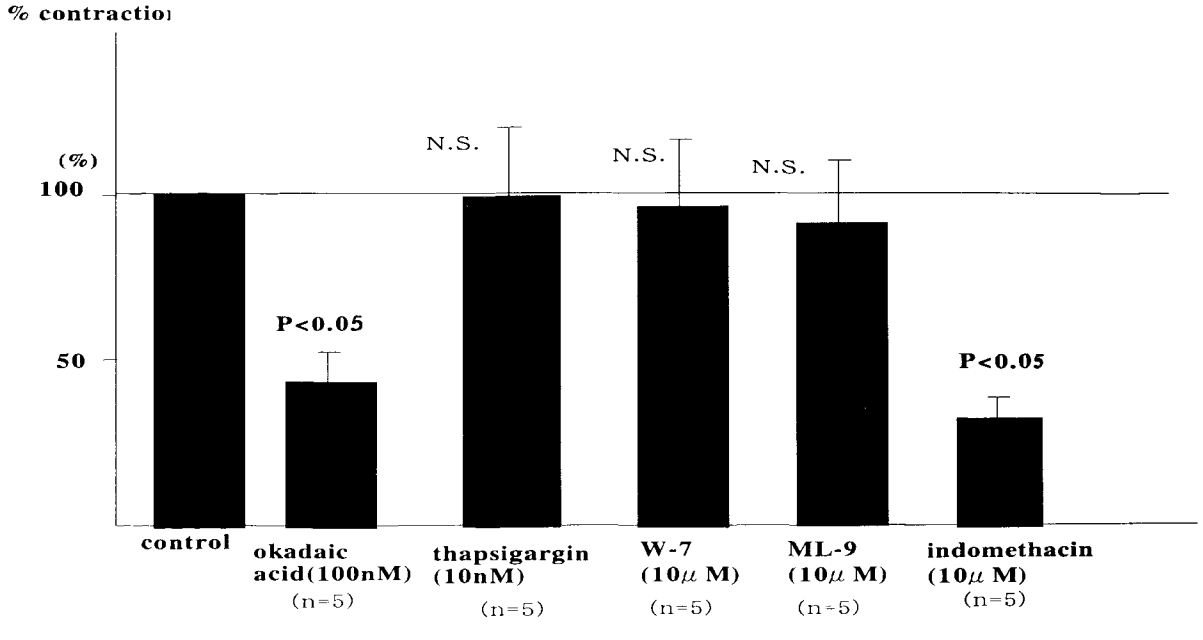
References

1) Brit. J Urol., 86:1-7, 2000.

showed no effect. During the contraction, PG E2 levels in the organ baths medium elevated significantly.



Inhibition effects for the re-perfusion contraction



Conclusions

The overactive contraction after ATP stimulation under a calcium free condition may be related to both the prostaglandin E2 receptor (EP1) and the membranous calcium influx mechanism.