

EFFECT OF CITRIC ACID ON RAT DETRUSOR MUSCLE CONTRACTION.

Hypothesis / aims of study

Leicestershire MRC Incontinence Programme (1), an epidemiological study has found daily consumption of carbonated soft drinks to be independently associated with the onset of OAB symptoms in the next twelve months (OR 1.62, 95% CI 1.18, 2.22). We therefore investigated the hypothesis that constituents of carbonated soft drinks modulate detrusor muscle function. Citric acid being one of the components may play an important role.

Study design, materials and methods

Bladders were removed from male and female Wistar rats (150g-300g) which have been culled in accordance with schedule 1 procedure of the Animal (Scientific Procedures) Act 1986. Bladder muscle strips were suspended in an organ bath perfused with Krebs's solution at 37°C aerated with 95% oxygen and 5% carbon dioxide. The apex of the muscle strip was attached to an isometric transducer connected to a four-channel oscillograph. Electrical field stimulation (EFS) was delivered by platinum electrodes recessed within the organ bath chamber and connected to a Harvard Dual Impedance Research Stimulator. The effect of increasing concentrations 10^{-8} M – 10^{-2} M of citric acid on the contractile response to a single frequency (10 Hz) of electrical field stimulation was determined. Those concentrations found to affect muscle contraction were investigated for their effect on EFS (0.5 Hz to 60 Hz), in the presence and absence of atropine 10^{-6} M. The effects of citric acid on responses to α , β -methylene ATP 10^{-3} M – 10^{-7} M, KCl (10mM – 80mM) and carbachol 10^{-8} M – 10^{-2} M were also determined.

Statistical analysis was determined by using Students t test where appropriate. A value of $p < 0.05$ was considered significant. Each graph is the mean plus SEM of six different experiments.

Results

Citric acid 10^{-5} M significantly enhanced the contractile response of rat detrusor muscle to 10 Hz EFS by 13.3% (< 0.05). The atropine resistance response to 40 Hz EFS was also increased by 10% (< 0.01) in presence of citric acid 10^{-5} M compared to control. The maximal contractile response to α , β -methylene ATP 10^{-3} M was increased by 15.8% (< 0.001) and the contractile response to KCl (70mM) was enhanced by 38% (< 0.01) in presence of citric acid 10^{-5} M compared to control. Citric acid 10^{-5} M however didn't modulate the maximum contractile response to carbachol significantly.

Interpretation of results

Citric acid enhanced the amplitude of the contractile response of rat bladder muscle. It appears to enhance the Ca^{+2} influx through L-type Ca^{+2} channels as demonstrated by its effect on the response to KCl. This may also be its mechanism of action on the atropine resistant component to EFS (ATP), and the direct enhancing effect on the maximal contractile response to $\alpha\beta$ methylene ATP.

Concluding message

Citric acid is an important component of many carbonated soft drinks. It is likely that citric acid along with other components of soft drinks, may have direct effects on bladder function as demonstrated so far in our study.