TRPV4 in rat myometrium contractility

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In recent years the importance at the study of the participation of ion channels in regulatory and signaling pathways both as effectors and as mediators, a lot consideration is given to transient receptor channels of potential (TRP), the expression of which is described for epithelial, smooth muscle and nerve cells [1]. Also the urgent problem such as preterm labor, that included premature birth of babies (globally near 10% average) and its increasing in most countries with reliable time trend data requires new avenues in understanding its mechanisms and potent therapy including investigation of the role TRPV4 in this problem.

The strips of rat uterine smooth muscle (myometrium) on 19-22 days of pregnancy were affected by Oxytocin, 10 nM (Gedeon Richter,Hungary), selective TRPPV4 agonist GSK1016790A? 0.3 μM (Sigma, USA), selective TRPV4 antagonist HC067047, 1 μM (Sigma, USA). Modified Krebs solution and hypotonic Krebs solution were used to perfuse muscle strips. Experiments were conducted on the research-tissue bath with force transducers, which was assembled at the department of Biophysics in KNU, the force contraction was recorded by force sensors, ADC and its related software. Studies of the contractile function of myometrium were performed by the method tensometry on several groups of smooth muscle preparations. This method register the muscle's contraction in isometric mode [2]. This study was approved by Institutional Bioethics committee.

Application of the selective TRPV4 channels agonist reduced force of phasic contractions by 26% ($p<0.05$). Duration of contractions was calculated at 50% of peak force and showed the increase up to 30%, without statistically significant difference. Area under the curve was reduced by up to 22% ($p<0.05$). These results indicate that there is a possible mechanism for reducing the excitability of uterus with the progress of labor, which could serve for protection of both the fetus and the organ. Probable mechanism of this phenomenon may include the activation of BK_{Ca} cannels, which, in turn, cause hyperpolarization of the myocytes plasma membrane [3]. Further electrophysiological studies are needed to address this hypothesis.

In experiments with hypotonic environment that was chosen as model of such pathologic conditions as hypertonic disease, diabetes and preeclampsia and activate mechanosensitive channels, myometrium strips responded with enforced contractibility, with the increase of fore amplitude up to 60% ($p<0.05$). TRPV4 by being sensitive to the cell stretch could also be involved in this phenomenon.

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