[S-031] Both OTR Antagonists, Atosiban and Nolasiban, Inhibits PGE_2/$PGF_{2\alpha}$-Induced Contractions of Human Pregnant Myometrium *In Vitro*.

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INTRODUCTION: Currently the only drug licensed in Europe for inhibition of preterm contractions is the intravenous oxytocin (OT)/ arginine vasopressin receptor antagonist Atosiban. Nolasiban is a more selective OT receptor antagonist (OTR-As) than Atosiban and may be administered orally. Prostaglandins (PG) also play key roles in cervical ripening and myometrial contractility and inhibition of PG synthesis or action has been used to delay preterm birth. Targeting the PG receptors or in combination with PG receptor antagonists and OTR-A may therefore be a more effective strategy for preventing or delaying preterm delivery. Previously we have shown that Nolasiban is more effective than Atosiban and that it inhibits spontaneous as well as OT-stimulated contractions. Here we examined the effects of Atosiban and Nolasiban on PGE_2/$PGF_{2\alpha}$-induced contractions of human pregnant myometrium.

METHODS: Experiments were performed using a DMT Myograph 800MS in oxygenated Kreb's solution, with ADI Powerlab software.Once regular contractions had been established for 20 min baseline measurement of contraction frequency, contraction peak, contraction duration, work per contraction and total work were made. The inhibitor compound was then added (6, 60 or 600nM), its effects upon spontaneous contractility measured in the next 10 min. The effect of the inhibitor upon agonist (PGE_2/$PGF_{2\alpha}$) was then measured by adding increasing concentrations of PGE_2/$PGF_{2\alpha}$ (1, 10, and 100nM) at 10 min intervals.

RESULTS: Atosiban antagonized the effects of $PGF_{2\alpha}$ upon the rate of contractions and contraction duration in a dose-dependent manner. Nolasiban inhibited $PGF_{2\alpha}$-induced contractions affecting rate, peak tension, and contraction duration therefore having an overall effect upon total work done. Nolasiban suppressed the effect of $PGF_{2\alpha}$ in a dose-dependent manner, reaching statistical significance at 600nM. Both Atosiban and Nolasiban reduced the effect of PGE_2 to similar extent.

CONCLUSIONS: In conclusion, our findings provide first evidence for receptor crosstalk between OTR and PG receptors which introduces a potential combinational therapeutic target for the management of term and preterm labour via the manipulation of the differential GPCR interactions/crosstalk.

Session: Poster Session: Basic Parturition (9:00 AM-10:30 AM)
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