In-Vitro Contractions of Pregnant Rat Myometrium Pretreated with Oxytocin: Comparison of Various Combinations of Uterotonic Agents

Abstract Type: Original Research
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Introduction: Oxytocin receptors in both human and rat myometrial cells are desensitized by exposure to oxytocin, reducing the ability of cells to respond to subsequent administration of oxytocin. This desensitization phenomenon is confined to oxytocin, and does not affect the actions of ergonovine and prostaglandin (PG) F2α. Oxytocin is frequently used in association with ergonovine and carboprost in the clinical setting with inconsistent results. The objective of this study was to investigate the effects of the combination of oxytocin with either ergonovine or PGF2α in oxytocin pretreated rat uterus.

Methods: After approval by the Animal Care Committee, the study was conducted in 32 pregnant Wistar rats at 21-22 days of gestation. Four longitudinal myometrial strips were isolated from each animal and allowed to equilibrate in separate 10ml organ bath chambers containing physiological salt solution (PSS) at 1g tension. The myometrial strips were pre-treated with either oxytocin 10⁻⁸M (experimental group; n=59) or PSS (control group; n=51) for 1h, then subjected to a dose-response study with oxytocin (cumulative increase from 10⁻¹⁰ to 10⁻⁵M) alone or in the presence of a constant concentration (10⁻⁹, 10⁻⁷ or 10⁻⁵M) of either ergonovine or PGF2α. The amplitude, frequency and motility index (amp x freq) of contractions during the dose-response period were analyzed using mixed linear modeling and compared among the groups.

Results: The motility index of myometrial contractions during the dose-response period in comparison to baseline values for experimental and control groups are shown in Fig 1. Oxytocin pretreatment significantly suppressed the myometrial contractions when the strips were further subjected to oxytocin or its combination with either ergonovine or PGF2α. A combination of ergot-oxytocin without oxytocin pretreatment produced superior contractions as compared to all other groups, while oxytocin alone in oxytocin pretreated myometrial strips produced weakest contractions (p=0.05) (Fig 1).

Discussion: A combination of oxytocin with ergonovine produces superior contractions compared to oxytocin alone or in combination with PGF2α, especially when the myometrium is pretreated with oxytocin. Should these data be replicated in human myometrium, it will have important clinical implications in the management of postpartum hemorrhage.

Dose response curves for motility index in various study groups

Logarithm of [motility index/(Baseline motility index)]

Oxytocin Concentration (M)

Ergot + Oxytocin (PSS pretreatment)
PGF2α + Oxytocin (Oxytocin pretreatment)
Ergot + Oxytocin (Oxytocin pretreatment)
PGF2α + Oxytocin (PSS pretreatment)
Oxytocin only (PSS pretreatment)
Oxytocin only (Oxytocin pretreatment)