

Effects of lindane and FeCl₃/ADP on spontaneous contractions in isolated pregnant rat and human term non-labouring myometrium

D. P. Champion¹, R. A. Fanning², M. O'Shea³, M. F. Carey², J. J. O'Connor³. ¹UCD School of Veterinary Medicine, University College Dublin, Dublin, Ireland, ²Department of Perioperative Medicine, Coombe Women and Infants University Hospital, Dublin, Ireland, ³UCD School of Biomolecular and Biomedical Science, University College Dublin, Dublin, Ireland.

Introduction: Labour is known to increase the production of reactive oxygen species (ROS), which are normally removed by antioxidant defence systems (1). Toxicants known to produce ROS, such as the organophosphate gamma-hexachlorocyclohexane (lindane), can cause oxidative stress and have been shown to inhibit spontaneous smooth muscle contraction (2). In this study we examined the effects of the oxygen species scavengers, ascorbic acid and N-acetylcysteine (NAC) on lindane and FeCl₃/ADP's inhibition of spontaneous myometrial contractions in rat and human myometrium.

Method: Myometrial biopsies were obtained from non-labouring women undergoing elective lower segment caesarean delivery. All patients were American Society of Anesthesiologists physical status 1/2 women and had given written informed consent. Ethical approval was obtained from the Research Ethics Committee of the Coombe Women and Infants University Hospital. In addition, with appropriate institutional research ethical approval, myometrial tissues were obtained from non-labouring, primigravida pregnant Wistar rats of gestational age 19-20 days. Myometrial tissue strips were dissected and individually mounted in organ baths, bathed in physiological saline maintained at 37°C and gassed with a 95% O₂/5% CO₂ mixture. Spontaneous contraction amplitude (g) and motility index (amplitude (g) x frequency) were recorded. The following protocols were used: (a) time-matched control (b) cumulatively increasing concentrations of lindane or FeCl₃/ADP or (c) cumulatively increasing concentrations of lindane or FeCl₃/ADP in the presence of NAC (1x10⁻⁴M) or ascorbic acid (1x10⁻⁴M). Non-linear regression statistical analysis was carried out [log (inhibitor) versus response (three parameters)] using GraphPad Prism v5. One-way ANOVA with *post hoc* Dunnett's test were used to compare the individual effects of the antioxidants versus lindane and FeCl₃/ADP in human and rat tissue.

Results: Lindane and FeCl₃/ADP treatment caused concentration-dependent reductions in rat (EC₅₀ 11.8x10⁻⁶ M and 0.9x10⁻³ M, N=6) and human myometrial motility (EC₅₀ 16.3x10⁻⁶ M and 1.1x10⁻³ M respectively, N=5). In the presence of NAC, there was a significantly increased EC₅₀ for the effects of lindane on motility index of human tissue (40.5x10⁻⁶ M, N=5, p<0.05). NAC also ameliorated the inhibitory effect of FeCl₃/ADP on contractions in both rat and human myometrium. The presence of ascorbic acid ameliorated the negative effects of FeCl₃/ADP in rat tissue only.

Conclusion: Lindane and FeCl₃/ADP reduced the contractility of both rat and human myometrium and specific antioxidants demonstrated a protective effect against this oxidative stress.

References:

1. Agarwal A *et al.* (2005) *Reprod Biol Endocrinol* **3**: 28.
2. Criswell KA and Loch-Carus R (1999). *Reprod Toxicol* **13**: 481-490.