Alteration of the Mare’s Immune System by the Synthetic Progestin, Altrenogest

O.F. Walker¹, C.E. Fedorka², B.A. Ball², A.A. Adams²

¹College of Veterinary Medicine, Lincoln Memorial University, Harrogate, TN, USA
²Department of Veterinary Science, University of Kentucky, Lexington, KY, USA

Abstract

Studies have shown that progestin (P4) and synthetic metabolites of progesterone have the ability to alter the immune system of various species.

- Altrenogest (ALT) is a synthetic form of P4 most commonly administered to horses primarily in order to influence reproductive physiology.
- Administration of such compound has been shown to increase the risk of uterine inflammation during early diestrus along with other physiological complications.

Peripheral blood mononuclear cells (PBMCs) were collected and isolated from 10 mares in diestrus. These cells were then incubated after the addition of various concentrations of P4 and ALT (10⁻¹M, 10⁻²M, 10⁻³M, 10⁻⁴M).
- Dexamethasone (DEX) was added at a concentration of 10⁻¹ to act as the positive control.
- Ethanol was used as the vehicle for incubation and served as the negative control.

After incubation, the cells were assessed in order to measure production and expression of key inflammatory cytokines (interleukins (IL)-1β, IL-6, IL-8, IL-10, IL-12, Tumor Necrosis Factor (TNF), and Interferon-Gamma (IFN-γ)).

This study revealed that both P4 and ALT caused a dose dependent decrease in the mRNA expression of IFN-γ and the anti-inflammatory cytokines IL-4, IL-6, and IL-10.

Results: Flow cytometry for IFN-γ

Ten non-pregnant mares in diestrus were selected at random and heparinized blood was collected for Peripheral Blood Mononuclear Cell (PBMC) isolation. These PBMC’s were then exposed to individual concentrations of P4, ALT, DEX, and a vehicle control, incubated, and later stimulated with Brefeldin A, phorbol 12-myristate 13-acetate (PMA), and ionomycin for further analysis via flow cytometry and quantitative polymerase chain reaction (qPCR).

Results: qPCR for IL-1b and IL-6

Exposure to altrenogest caused a dose-dependent increase of mRNA expression of pro-inflammatory cytokine IL-1b and the inflammatory modulating cytokine IL-6. Progesterone treatment proved to have insignificant effects.

Discussion/Future Directions

Discussion:
Our data showed that in vitro altrenogest administration altered the cellular immune response of the non-pregnant mare, and this was at times in contrast to progesterone. A similar result is seen in other species, where synthetic progestins are found to increase the production and expression of pro-inflammatory cytokines, and this is believed to predispose women to various diseases.

Future directions:
IT is unknown if exposure to altrenogest increases disease risk in the mare, but the results from this study indicate a similar alteration on the immune system, justifying future research to evaluate the effect of altrenogest on diseases such as placentalitis and leptospirosis.

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