Efficacy of gonadorelin hydrochloride or gonadorelin diacetate tetrahydrate 7 days after AI in field conditions to boost progesterone levels, a randomized clinical trial

V. Caldwell, *DMV, MSc*[1]; **R. Martineau**, *DMV, PhD*[2]
[1]*Clinique vétérinaire de Coaticook, Coaticook, Québec, Canada J1A 1P9*
[2]*Centre de recherche sur le bovin laitier et le porc, Sherbrooke, Québec, Canada J1M 0C8*

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Introduction

The ability of some reproduction synchronization protocols to increase conception rates (CR) is reported as being in part due to increased progesterone (P4) levels in the diestrus phase before breeding. This has been demonstrated mostly in an experimental context and was linked to GnRH increasing the proportion of cows luteinizing a second corpus luteum (CL). A pilot trial was conducted to determine if an injection of gonadorelin hydrochloride (Factrel®) or gonadorelin diacetate tetrahydrate (Cystorelin®) given 7 days after AI to all cows on a farm in field conditions resulted in a significant increase of P4 levels 14 days after AI, compared to a placebo. If an increase in P4 levels was to be observed, a second larger trial was to be conducted testing the effect of post-AI GnRH on CR at return to estrus.

Materials and Methods

A commercial dairy herd (275 lactating Holstein cows, free-stall, average daily milk: 79.2 lb (36 kg)/cow/day) was chosen in Quebec based on its high ability to rebreed cows on return to estrus (using an activity monitor and visual observation, 42% of open cows rebred between 19 and 23 days post AI). Conception rate during the study was 34% and the 21-day pregnancy rate was 25%. A targeted number of 120 cows (3 groups of 40 cows) were recruited to detect a difference of 1.5 ng/ml of serum P4 in cows having received either GnRH or a placebo (sterile water), alpha and beta errors being 0.05 and 0.15, respectively. The dairy operator was instructed to inject all inseminated cows 7 days after AI with 2 ml from 3 identical bottles alternately and was blinded to treatments. All AIs were to be enrolled, notwithstanding AI number and type of estrus (natural or synchronized). Blood was collected from all cows 7 days after treatment (14 days after AI) and refrigerated. All blood samples were centrifuged within 2 days and frozen immediately. Serum samples were analyzed for P4 at the Ontario Veterinary College in Guelph at the end of the trial, on 1 same day. One-way analysis of variance was used to compare P4 levels between placebo and each GnRH product.

Results

The study began May 7, 2015, and ended July 5, 2015. Means (±SD) of P4 for each treatment were 6.61 ± 2.42 ng/ml (n=38), 7.28 ± 1.82 ng/ml (n=42), and 6.67 ± 2.08 ng/ml (n=40) for placebo, Factrel® and Cystorelin®, respectively. No difference was observed between Factrel® and placebo (P=0.16) or Cystorelin® and placebo (P=0.91).

Significance

The variability in P4 levels in our study (SD=2.17 ng/ml) was greater than it was in 3 other similar studies where P4 levels were measured following GnRH injection 7 days after AI (average SD=1.74 ng/ml) (Dolezel et al, 2013, Musilova et al, 2014, Howard et al, 2006). The numerical difference in mean P4 levels between placebo and GnRH treatment groups was smaller in our study (0.67 ng/ml for Factrel® and 0.01 ng/ml for Cystorelin®) than it was in the aforementioned 3 studies (average difference=1.59 ng/ml). Under the field conditions of our study, some animals submitted to AI were possibly not in true estrus and, therefore, not injected at the optimal moment of their cycle to respond to GnRH and luteinize a second CL. However, these field conditions are those in which the authors wished to see if GnRH could eventually increase CR at the next breeding, hence this study provides valuable information to them. No conclusion can be reached by comparing mean P4 levels between the Factrel® and Cystorelin® groups, which was not the goal of this study. If the goal had been to compare the efficacy of the 2 GnRHs, a much greater sample would have been needed because the expected difference in P4 levels between GnRHs would have been much smaller compared to the difference in P4 levels between GnRH and placebo-treated cows. Having detected no significant difference in P4 levels in these field conditions, the authors decided not to go forward with the next study, whose aim was to test the effect of GnRH 7 days after AI on CR at return to estrus.