

## ADRENOCORTICAL RESPONSE IN COWS AFTER INJECTION OF ADRENOCORTICOTROPIC HORMONE

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### ***Abstract***

*Adrenocorticotrophic hormone (ACTH) challenge test is recognized as a method for evaluating some forms of stress. Six lactating cows, well trained to blood sampling were used for this study. Cows were randomly assigned to receive saline or an intramuscular single dose (0.5 µg/kg) of ACTH (Synacthen Depot). Blood samples (10 mL) were collected from the coccygeal blood vessels of all cows at 0 h (immediately before treatment) and every 30 min for 2 h to measure serum cortisol, glucose, creatinine and urea concentrations. Each blood collection included a separate puncture of the coccygeal blood vessels using a new needle. Respiratory frequency was measured for each cow at 0, 30, 60, 90 and 120 min. Serum cortisol concentrations of cows did not differ between treatments at the initiation of treatments; however, serum cortisol, glucose, creatinine, urea concentrations and respiratory frequency were affected by ACTH, time, and the interaction of ACTH x time. Administration of ACTH increased ( $P < 0.05$ ) serum cortisol concentration in cows within 30 min of administration, and concentrations remained increased through the blood sampling period. Cows that received ACTH had increased ( $P < 0.05$ ) respiratory frequency within 30 min of administration. An increase in hypothalamic pituitary-adrenocortical activity, causes the rise of blood cortisol, indicates a physiological response to different stressors.*

**Key words:** *adrenocorticotrophic hormone, cortisol, cow.*

### **INTRODUCTION**

Adrenocorticotropin (ACTH) is a polypeptide hormone composed of 39 amino acids that is secreted by corticotroph cells in the anterior pituitary gland. Since they share the same receptor in the adrenal gland the sequence ACTH<sub>1-24</sub> (Synacthen) has the same biological action as the whole molecule. Assessment of serum cortisol levels following the administration of adrenocorticotrophic hormone is a recognised method for evaluating adrenal cortex function in human and veterinary clinical medicine (Verkerk et al., 1994; Pacak and Palkovits, 2001). Larger doses of ACTH are needed if the researcher wishes to maintain serum cortisol for a longer time period (Lay et al., 1996).

The aim of this study was to determine the adrenocortical response of Holstein-Friesian mix breed cows to a single dose of ACTH (Synacthen) as Tetracosactide Hexaacetate. Another objective was to examine the relationship between changes in cortisol concentrations in serum and some biochemical parameters, following activation of the hypothalamic-pituitary-adrenocortical axis.

## **MATERIALS AND METHODS**

Six lactating cows, well trained to blood sampling were used for this study. Cows were randomly assigned to receive saline or an intramuscular single dose (0.5 µg/kg) of ACTH (Synacthen Depot 1mg/mL). Blood samples (10 mL) were collected from the coccygeal blood vessels of all cows at 0 h (immediately before treatment) and every 30 min for 2 h to measure serum cortisol, glucose, creatinine and urea concentrations with an automatic biochemistry device Cormay Accent 200. Each blood collection included a separate puncture of the coccygeal blood vessels using a new needle. Respiratory frequency was measured for each cow at 0, 30, 60, 90 and 120 min. For the statistical evaluation, SPSS 16.0 for Windows was used. The statistical analysis was made using t-test and Pearson correlations.

## **RESULTS AND DISCUSSIONS**

Peak cortisol, the increment of peak above basal cortisol level, and the integrated cortisol response over time following ACTH treatment are used as measures of adrenocortical responsiveness (Bertoni et al., 2005).

In our study cortisol levels measured before and after ACTH injections in cows are shown in Figure 1. Compared to baseline (samples 0 min), serum cortisol increased significantly after ACTH administration to reach their maximal levels at 30 min and peak concentrations were on average 14 to 19 times greater than basal concentrations. In general, our results were similar to those observed by other authors in calves after ACTH administration (Veissier et al., 1999) and in cows during and after machine milking (Gorewit et al., 1992; Rushen et al., 2001; Negrao et al., 2004; Knights et Smith, 2007). Mean serum cortisol response was greater ( $P < 0.005$ ) in all ACTH-treated cows than in saline-treated cows at 30, 60, 90 and 120 min.

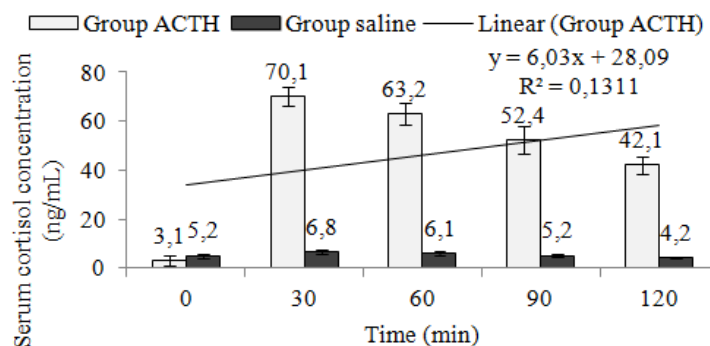


Figure 1. Mean serum cortisol concentrations for cows administered with saline (2 mL, 0.9% NaCl) or 0.5 µg of ACTH/kg BW

Typical metabolic consequence of cortisol is to increase blood sugar through gluconeogenesis (Desborough, 2000) and to increase respiratory rate (Schubert et al, 2009). Serum glucose (Figure 2) concentration of cows did not differ ( $P=0.48$ ) between treatments at the initiation of treatment (time 0); however serum glucose was affected ( $P=0.05$ ) by ACTH, time and the interaction of ACTH x time. Administration of ACTH increased serum glucose concentration.

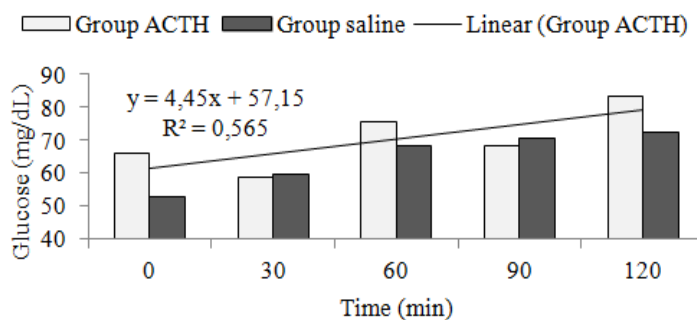


Figure 2. Mean serum glucose concentrations for cows administered with saline (2 mL, 0.9% NaCl) or 0.5 µg of ACTH/kg BW

Respiratory frequency value with (Group ACTH) and without (Group saline) ACTH treatment are summarized in Figure 3. Difference between Group ACTH and Group saline were not statistically significant ( $P>0.05$ ). Respiratory frequency reached the maximal levels at 30 min after ACTH

administration followed by a decrease till the end of study. Study revealed a direct correlation ( $P=0.001$ ,  $r=0.991$ ) between serum cortisol and respiratory frequency.

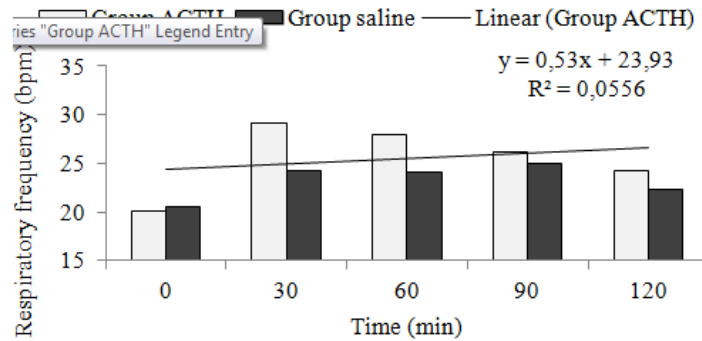


Figure 3. Mean respiratory frequency for cows administered with saline (2 mL, 0.9% NaCl) or 0.5 µg of ACTH/kg BW

Cortisol is known also to increase blood pressure, having a direct renal actions resulting in vasodilatation One possible mechanism is the reported increase in renal vascular resistance (Xe et al., 2006).

Urea and creatinine concentration are tests done to monitor kidney function. Serum urea and creatinine value with (Group ACTH) and without (Group saline) ACTH treatment are summarized in Figure 4 and 5. Difference between Group ACTH and Group saline values were not statistically significant ( $P>0.05$ ). During the entire study, the urea and creatinine were placed in physiological limits for cows. Pearson statistical test showed no correlation between evolution of cortisol and urea.

Regarding creatinine concentration, the most elevated values were observed before the ACTH treatment ( $1.19 \pm 0.02$  mg/dL) and the lowest in those 30 min after the treatment ( $0.74 \pm 0.09$  mg/dL), but the differences were not statistically significant ( $P> 0.05$ ).

Study revealed an indirect correlation ( $P=0.01$ ,  $r=-0.933$ ) between serum cortisol and creatinine.

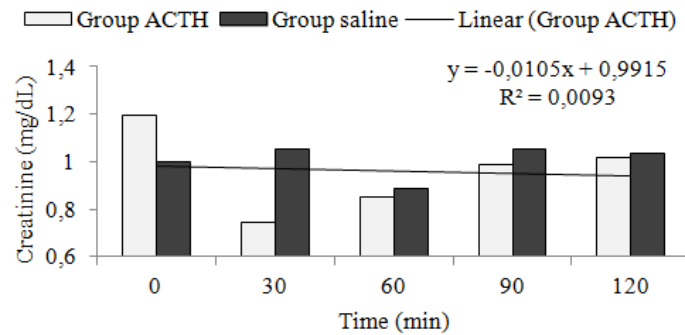


Figure 4. Mean serum creatinine concentrations for cows administered with saline (2 mL, 0.9% NaCl) or 0.5 µg of ACTH/kg BW

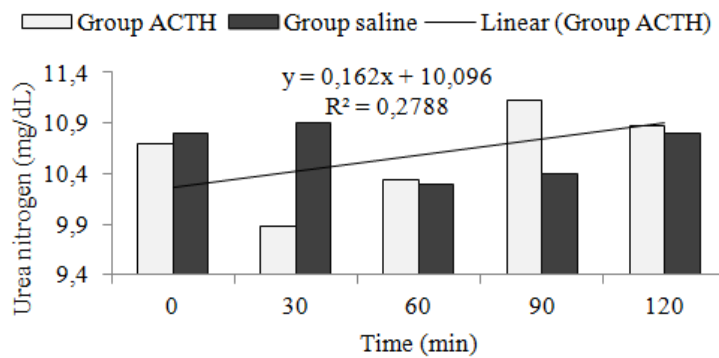


Figure 5. Mean serum urea nitrogen concentrations for cows administered with saline (2 mL, 0.9% NaCl) or 0.5 µg of ACTH/kg BW

## CONCLUSIONS

Administration of ACTH increased ( $P < 0.05$ ) serum cortisol concentrations in cows within 30 min of administration, and concentrations remained increased throughout the blood sampling period.

Cows that received ACTH had increased ( $P < 0.05$ ) respiratory frequency within 30 min of administration.

Study revealed a direct correlation ( $P = 0.001$ ,  $r = 0.991$ ) between serum cortisol and respiratory frequency, and an indirect correlation ( $P = 0.01$ ,  $r = -0.933$ ) between serum cortisol and creatinine.

Administration of ACTH at the dose rate of 0.5 µg ACTH/kg of body weight will induce cortisol release and may be used to test the sensitivity of the adrenal gland during different stressors.

## ACKNOWLEDGEMENTS

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