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Serum Cortisol Concentrations in Response to Ovario-hysterectomy and Following Post-operative Analgesia with Carprofen and Meloxicam in Dogs

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ABSTRACT

Serum cortisol levels following ovario-hysterectomy and post-operative analgesia with carprofen and meloxicam were studied in twelve dogs randomly assigned to Group A and Group B. In Group A, carprofen was administered @ 4 mg/kg i.v, whereas in Group B, meloxicam was administered @ 0.2 mg/ kg i.v, immediately after completion of surgery. Study revealed that the cortisol levels increased up to 6 to 7 fold immediately after ovariohysterectomy. Induction of analgesia with carprofen and meloxicam significantly reduced the level of cortisol. Carprofen was found to be a better analgesic than meloxicam in terms of its role in reducing the cortisol levels post-operatively.

Keywords: *Cortisol, carprofen, meloxicam, dog*

Management of pain is one of the most challenging problems in veterinary medicine. Pain is not only unacceptable under the ethics of animal care (Smith, 2005), but it also inhibits optimal recovery after trauma (Ferguson, 1995). Serum cortisol in blood has been widely used as a biochemical marker of stress and pain (Smith *et al.*, 1999) produced following noxious stimulus or surgical stresses such as following ovariohysterectomy in dogs. Significant pain is caused following ovariohysterectomy which can apparently be relieved by using different combination of opioid or non-steroidal anti-inflammatory drugs (Fox *et al.*, 2000). Non-steroidal anti-inflammatory drugs, preferably COX-2 enzyme inhibitors have lower risk of side effects (Papich, 2000) and currently approved for use in veterinary patients include meloxicam, carprofen, ketoprofen and etodolac (Forsyth *et al.*, 1998, Mathews, 2000 and Moreau *et al.*, 2003). Both carprofen and meloxicam besides being analgesic also have antipyretic and anti-inflammatory properties. Biochemical markers such as cortisol and glucose are commonly used as an indirect measure of pain (Fox *et al.*, 1994). Marked increase in cortisol concentration has been reported after variety of surgical procedures (Dodman *et al.*, 1990). The present study was therefore conducted to compare the effect of carprofen and meloxicam in lowering the levels of cortisol in ovario-hysterectomized dogs.

MATERIALS AND METHODS

Twelve clinically healthy dogs brought for elective ovario-hysterectomy were randomly divided into two groups comprising six animals each. All the animals were pre-medicated with atropine sulphate @ 0.04 mg/kg i.m, and 30 minutes later by administration of diazepam @0.5 mg/ kg slow i.v. Anaesthesia was induced with 5%

solution of thiopentone sodium as i.v bolus administration "to effect". The anaesthesia was maintained by incremental doses of thiopentone sodium as and when required.

On the day of surgery, the animals were randomly assigned to Group A and Group B.

Group A: Six dogs were administered Carprofen @ 4 mg/kg i.v, immediately after completion of the surgical procedure.

Group B: Six dogs were administered meloxicam @ 0.2 mg/kg i.v, immediately after completion of the surgical procedure.

SURGICAL PROCEDURE

Ovario-hysterectomy was performed *via* ventral mid-line approach as per the standard surgical procedure described by Bojrab, 1997. The surgical technique, surgeon, length of skin incision and post-operative care was kept uniform for all the animals. Venous blood samples were collected before administration of anaesthesia and at each examination viz., immediately after surgery, and at 12 and 24 hours post-operatively. Blood was transferred in a vial without anticoagulant and was allowed to clot. Serum harvested from blood was used for estimation of cortisol.

RESULTS AND DISCUSSION

During the study uniformity was maintained among groups with regard to average body weight, anaesthetic protocol, length of incision, surgical procedure and the time taken in the surgery to minimize the difference in level of pain that would arise due to different body weight, anaesthesia, length of incision, surgical procedure and the time taken in the surgical procedure. The surgical procedure and recording of the observations in all the animals was done by the same surgeon. Gupta, 2007 also suggested maintaining uniformity with respect to body weight, anaesthetic technique and the surgical procedure to nullify their effects, while measuring pain in ovario-hysterectomized dogs. Some anaesthetics having residual analgesic property tend to mask the signs of pain at recovery, however, thiopentone that was used as anaesthetic in the dogs in the study is devoid of such post-anaesthetic analgesic property, and thus it tends to fail in masking the signs of pain at recovery.

Biochemical markers such as cortisol and glucose are commonly used as objective and indirect measures of pain (Fox *et al.*, 1994 and Hansen *et al.*, 1997). In the present study, a significant 6 to 7 fold increase ($P<0.05$) in cortisol level to 343.47± 10.77 nmol/l and 338.93± 23.90 nmol/l in group A and group B respectively was recorded immediately after surgery, from pre-operative value of 52.73 ± 3.20 nmol/l and 51.31± 5.23 nmol/l. The concentration of cortisol then gradually declined and by 24 hours post surgery it was 67.48 ± 1.68 nmol/l and 97.13 ± 5.79 nmol/l in group A and group B respectively, but was still higher when compared to pre-operative level (Fig.1).

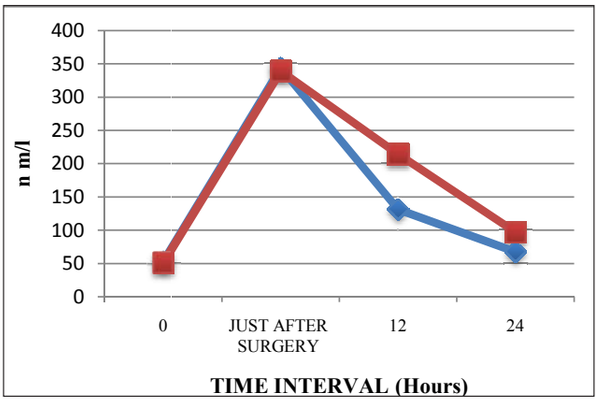

Fig. 1: Serum cortisol concentrations at different time intervals

Similar findings were reported by Fox *et al.* (1994) wherein very high concentration difference was recorded between the skin incision and manipulation of ovaries during ovariohysterectomy. The values between the groups also differed significantly ($P<0.05$) at 12 and 24 hours post-operatively with carprofen

decreasing the level of cortisol to a lower level than meloxicam.

Restraining, handling and isolation has been reported to cause hypercortisolemia in lambs (Minton and Blecha, 1990). Cortisol concentrations may also be increased due to direct effect of stress induced by general anaesthesia. Thiopental sodium and etomidate have been reported to increase plasma cortisol concentration after the induction of anaesthesia in dogs (Dodam *et al.*, 1990). Barbiturate anaesthesia maintained by halothane in bitches has resulted in hypercortisolemia (Fox *et al.*, 1994). Marked increase in cortisol concentration has also been reported following variety of surgical procedures conducted under general anaesthesia in dogs (Dodam *et al.*, 1990). Increased levels of cortisol recorded in the study can be attributed to induction of anaesthesia by thiopental sodium and/or surgical manipulations as afferent nerve impulses from surgical site act *via* hypothalamus to activate hormone secretion from hypothalamus-pituitary-adrenal axis (HPA) as well as sympatho-adrenal-medullary axis (Minton, 1994) causing increased secretion of ACTH from adenohypophysis. ACTH is a major hormone regulating the synthesis and secretion of glucocortcoids including cortisol from zona fasciculate and zona reticularis of adrenal cortex (Dantzer, 1983).

Decreased in cortisol levels at 12 and 24 hours post-operatively and significant decrease in Group A as compared to Group B shows that carprofen is more potent in reducing surgical stress as compared to meloxicam, although meloxicam also decreased the levels of cortisol at 12 and 24 hours post-operatively.

CONCLUSION

Study revealed that the cortisol levels increased up to 6 to 7 fold immediately after ovariohysterectomy. Induction of analgesia with carprofen and meloxicam significantly reduced the level of cortisol. Carprofen was found to be better analgesic than meloxicam in terms of its effect in reducing the cortisol levels post-operatively.

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