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An evaluation of serum prolactin in anxious dogs and response to treatment with selegiline or fluoxetine

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Abstract

Defining objective, reproducible and standardized parameters for the evaluation of patients is one of the main academic focuses of veterinary behaviour medicine. Prolactin, a peptidic neurohormone and a cytokine, whose main regulator is dopamine, seems to be of particular interest in relation to chronically distressed patients. The aim of this clinical study was to assess the correlation between prolactin levels in the blood (prolactinaemia) and chronic anxiety and to evaluate its value in helping to guide the choice of the most appropriate drug in dogs displaying emotional disorders. The inclusion criteria included an EDED score superior or equal to 10 and the absence of any previous treatment or physical condition, which could modify prolactin secretion or emotional reactions. After inclusion, a randomization number was assigned to the dog, with a preselected treatment: fluoxetine (1 mg/kg once a day) or selegiline (0.5 mg/kg once a day). Each dog was evaluated with a complete behaviour examination, a physical examination, EDED score and a blood sample to measure prolactinaemia.

The dogs were re-evaluated 4 weeks, 8 weeks and 16 weeks later. The follow-up visits were organised the same way as the inclusion visit, including EDED scoring and prolactinaemia evaluation.

A population of 84 dogs was enrolled in study. The analysis of the correlations between prolactinaemia and EDED score show a positive significant correlation.

Evaluation of treatment follow up showed a statistically significantly greater improvement with selegiline in the dogs with higher levels of prolactinaemia compared to those with lower levels of prolactin, who were significantly more improved by fluoxetine.

Keywords: Dog; Behavioural medicine; Anxiety; Prolactin; Selegiline; Fluoxetine

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1. Introduction

Anxiety is commonly diagnosed in canine behaviour medicine. The aetiology of anxiety is difficult to assess but it is commonly accepted that chronic ambivalent situations as well as inappropriate conditions of life can induce anxiety. Thus assessing anxiety is not only a medical question but also crucial in a welfare context. When a syndrome is characterized by emotional reactions of concern, it makes scientific sense to try to obtain objective measures such as blood testing for hormones or metabolites. Cortisol and related compounds were some of the first parameters used to assess distress and emotional disorders (Gibbons, 1964; Klemcke, 1994). Unfortunately, this hormone, released in a pulsatile pattern (Ladewig, 1987), shows significant individual variation, which makes it difficult to define a clinical reference value. Other hormones, thought to be part of emotional reactions, like thyroid hormones, have also been studied, but dramatic individual and interindividual variations as well as the necessity to establish a baseline, make their use difficult, usually poorly predictive in clinical setting and impractical to use during follow-up.

Some experimental researchers have focused their on pituitary hormones. Because they are directly under hypothalamic control, involving monoaminergic neurones, their variations are supposed to be more sensitive to any emotional modification. For example, ACTH, was one of the first to be used given its relationship with its activating releasing-factor (CRF) for cortisol and associated emotional reactions (Landfield, 1987; Kuroda et al., 1992; Bailly et al., 1993).

Among these pituitary hormones, prolactin (PRL) appears particularly interesting because of its inhibitory hypothalamic control. Secretion of most of the other pituitary hormones is determined by the stimulating action of hypothalamic releasing-factors, but the secretion of PRL is thought to be mainly mediated by the suppressive effects of dopamine (Ben-Jonathan, 1985). This does not exclude stimulatory control of PRL secretion; several substances like thyrotropin-releasing hormone (TRH), neurophysin, or substance P have been shown to stimulate its release (Kuan et al., 1990; Shin et al., 1995; Watanobe and Sasaki, 1995). Literature reports show that a variety of stressors increases the release of this hormone (Van de Kar et al., 1991). During controlled stress-eliciting assays, PRL rate shows a rapid increase reaching its maximum after 3 min and a slow decrease with a return to reference values reached after 60 min. In hyperemotional mice (Roman Low Avoidance), the PRL blood level remains higher after stress than in hypoemotional ones (Roman High Avoidance) (Castanon, 1992). In humans, different studies have shown a positive correlation between anxiety and serum prolactin (Jeffcoate et al., 1986; Turner et al., 2002). In pseudopregnant female dogs, serum prolactin is increased and their behaviour includes signs of anxiety, which disappear when they are treated using drugs, which stimulate dopamine release (Gobello et al., 2001a,b). In dogs suffering anxiety, some published data have shown some modification in the dopaminergic neurones (Reisner et al., 1996; Osella et al., 2002, 2005).

These data could be seen as strong arguments to use drugs, which stimulate dopaminergic receptors in the treatment of anxiety in dogs. On the contrary, literature shows very equivocal results regarding the efficacy of different drugs in the treatment of anxiety in dogs; especially when comparing serotonin re-uptake inhibitors (SSRI) and selegiline (a drug which increases dopamine release) (Overall, 1997; Pageat, 1998; Landsberg et al., 2003). Some anxious dogs, displaying the same symptoms, are improved by fluoxetine (an SSRI), and others are worsened by the same treatment but improved by selegiline. These results could suggest biological heterogeneity in the population of anxious dogs.