Acta Scientific Veterinary Sciences (ISSN: 2582-3183)

Volume 6 Issue 2 February 2024

Research Article

Comparative Assessment of Efficacy of Prednisolone and Cyclosporine in Canine Pemphigus Complex

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DOI: 10.31080/ASVS.2024.06.0823

Received: October 31, 2023

Published: January 24, 2024

Abstract

Background: Immunosuppressant is the mainstay of treatment in canine pemphigus infection and often the treatment is of chronic course in nature. Prolonged use of immunosuppressant leads to various adverse effects.

Objective: There is a need to study the comparative efficacy of immunosuppressant agents in canine pemphigus complex.

Methods: Dogs presented with clinical signs suggestive of pemphigus complex were enrolled into the study and diagnosed based on the acantholytic cells evidence in the cytology of skin impression smear and histomorphology. Dogs were randomly divided into two groups. Gr.1 was treated with Prednisolone @ 2mg/Kg PO (dose tapered later once in every 7 days for 3 weeks) and Gr. II was treated with Cyclosporine @ 5 mg/Kg PO for 3 weeks. Dogs were monitored for resolution of clinical signs and hematobiochemical changes during therapy.

Results: Prednisolone treated dogs showed faster response in contrast to cyclosporine group but, recurrence of clinical signs was noticed in few dogs when the dose was tapered. But, cyclosporine treated dogs responded favourably with mild gastric discomfort without any changes in the liver and kidney function markers. There was no significant difference in the complete blood count and vital organs markers (BUN, Creatinine, SGPT, and ALP) before and after therapy except blood glucose level.

Conclusion: Cyclosporine treated dogs responded favourably as compared to prednisolone treated dogs.

Keywords: Cyclosporine; Dogs; Immunosuppressant; Pemphigus; Prednisolone

Introduction

The epidermis consists of multiple layers of keratinocytes and makes up the outer layers of the skin. The keratinocytes in the epidermis are held together by desmosomes, which are cell-cell adhesion molecules made of several different proteins, such as desmocolin and desmoglein [1]. These adhesion molecules are frequent targets for autoimmune diseases and their destruction results in superficial blistering or acantholysis. Canine pemphigus foliaceus (PF) is one of the most common autoimmune dermatoses in dogs [2]. Pemphigus foliaceous is the most common autoimmune disease in dogs and is most often caused by autoantibodies targeting desmocollin-1 [3]. Currently, the diagnosis of canine PF is mainly based on clinical signs, cytology and histomorphology of skin lesions. ANA, IFA, IPS are choices of diagnostics but, often yields false positive results.

There are four different forms of pemphigus: pemphigus erythematosus (PE), pemphigus foliaceus (PF), and pemphigus vegetans (Pveg). Dogs rarely develop pemphigus vulgaris, which typically results in systemic disease. Pemphigus vegetans is incredibly uncommon and is assumed to be a milder form of PV. Immunosuppressant is the mainstay of the treatment and these agents have adverse effects with chronic usage [4]. The most commonly observed adverse effects are vomiting, diarrhoea, persistent otitis externa,

urinary tract infections, anorexia, lethargy, gingival hyperplasia, and lymphadenopathy [5], and the most common serum chemistry changes includes increased serum creatinine concentration [6,7], hyperglobulinemia, hyperphosphatemia, hyperproteinaemia, hypercholesterolemia, hypoalbuminemia [8], hypocalcaemia, and increased blood urea nitrogen concentration [9]. Identification of best immunosuppressant agent which can cause resolution of clinical signs without compromising the health of host is the need of hour. The present study aimed to compare the efficacy of prednisolone and cyclosporine in the naturally occurring canine pemphigus complex cases.

Methodology

Dogs presented to Referral Veterinary Polyclinic, ICAR- Indian Veterinary Research Institute, Izatnagar, Bareilly, Uttar Pradesh, India with clinical signs suggestive of pemphigus complex were enrolled in this study. Clinical examination exhibited scaling of skin, alopecia and ulceration at muco-cutaneous junction of face. For, confirmatory diagnosis, skin impression smear was prepared and subjected to Giemsa staining. Skin tissue samples were also collected by punch biopsy in few dogs and subjected to histomorphology using hematoxylin and eosin stain. Dogs presented with similar clinical signs and found positive for manage and fungal infection were excluded from this study and treated accordingly. Dogs affected with pemphigus foliaceus were randomly divided into two groups (n = 6). Gr.1 was treated with Tab. Prednisolone @ 2mg/Kg PO (dose tapered later once in every 7 days for 3 weeks) and Gr. II was treated with Cap. cyclosporine @ 5 mg/Kg PO for 3 weeks. Blood and serum samples were collected before and after the treatment to observe any changes in the vital organ function.

Statistical analysis

Independent sample't' test was employed to determine the statistical significance of blood parameters. The statistical analysis was considered significant at $p \leq 0.05$.

Results

Dogs presented with clinical signs presumptive of pemphigus were examined clinically and pemphigus foaliceus was diagnosed based on cytology of impression skin impression smear and skin histomorphology (Figure 1 and 2). Most of the dogs were in the middle age group and the body weight was 20 to 30 kilogram. Skin scraping was negative for mite and fungal infection in all the pemphigus positive dogs. Cytology of skin impression smear stained with Giemsa stain revealed characteristic acantholytic cells suggestive of pemphigus foliaceus infection. Histomorphology of skin sample revealed severe infiltration of inflammatory cells including neutrophils, lymphocyte and rounded acantholytic cells having eosinophilic cytoplasm. There was no significant difference in the complete blood count changes and vital organs markers (BUN, Creatinine, SGPT, ALP, and Glucose) before and after therapy except blood glucose level in the both the groups (Table 1-4). Study revealed that response to therapy was faster in prednisolone treated group whereas it was delayed in cyclosporine treated group. Inappetance and vomiting were recorded in few dogs treated with cyclosporine. In prednisolone treated groups, few dogs had showed recurrence of clinical when the dose was tapered.

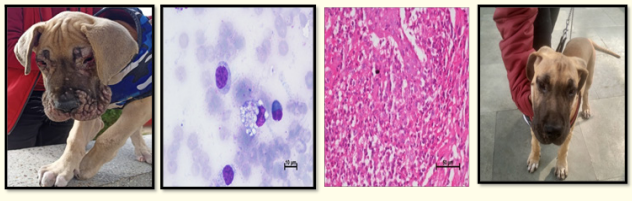

Figure 1: a Before treatment, b-Acantholytic cells in cytology, c-Histomorpholgy shows inflammatory cells with acantholytic cells, d- Recovered dog.

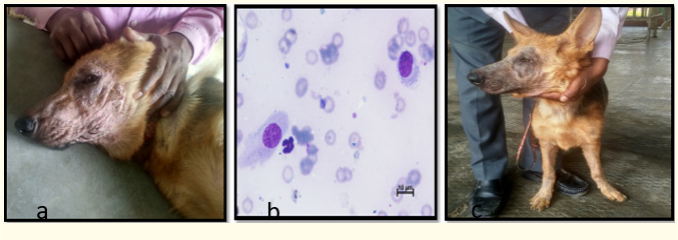

Figure 2: a-Before treatment, b-Acantholytic cells in cytology, c- Recovered dog.

Sr.No	Parameters	Before treatment (Mean + SD)	After treatment (Mean + SD)	Reference range	P value
1	Hb (g%)	10.98 ± 0.95	10.28 ± 0.57	12-19	0.197
2	PCV (%)	34.17 ± 2.4	34.17 ± 1.2	33-44	1.000
3	RBC × 10^{6}/cmm	5.7 ± 0.5	5.5 ± 0.4	5-7.9	0.225
4	WBC10^{3}/cmm	14791 ± 1710	13520 ± 1454	5000-14100	0.057

Table 1: Complete Blood Count changes in Prednisolone treated dog.

Sr. No	Parameters	Before treatment (Mean + SD)	After treatment (Mean + SD)	Reference range	P value
1	BUN (mg/dl)	16.4 ± 0.3	18.1 ± 2.1	8-23	0.42
2	Creatinine(mg/dl)	0.92 ± 0.1	1.01 ± 0.4	1.1a-2.2	0.43
3	SGPT (IU/L)	79 ± 15	67 ± 10	10-109	0.16
4	Glucose (mg/dl)	78 ± 3.9	83 ± 3.3	60-120	0.004

Table 2: Serum Biochemicals changes in Prednisolone treated dog.

Sr. No	Parameters	Before treatment (Mean + SD)	After treatment (Mean + SD)	Reference range	P value
1	Hb (g%)	11.16 ± 0.7	11.2 ± 0.6	12-19	0.93
2	PCV (%)	33.5 ± 1.6	33.6 ± 1.3	33-44	0.86
3	RBC×10^{6}/cmm	5.6 ± 0.5	5.5 ± 0.3	5-7.9	0.57
4	WBC10^{3}/cmm	11516 ± 1770	11676 ± 1419	5000-14100	0.76

Table 3: Complete Blood Count changes in Cyclosporine treated dog.

Sr. No	Parameters	Before treatment (Mean + SD)	After treatment (Mean + SD)	Reference range	P value
1	BUN (mg/dl)	19.9 ± 0.9	27.5 ± 8.9	8-23	0.42
2	Creatinine(mg/dl)	1.08 ± 0.1	1.16 ± 0.2	1.1-2.2	0.36
3	SGPT (IU/L)	77 ± 3.3	76 ± 2.8	10-109	0.9
4	Glucose (mg/dl)	84 ± 1.7	89 ± 1.7	60-120	0.013

Table 4: Serum Biochemicals changes in Cyclosporine treated dog.

Discussion

Canine pemphigus foliaceus (PF) is one of the most common autoimmune disorders in dogs and immunosuppressant is the mainstay of the therapeutic regimen. Many immunosuppressant agents are available and each has its merits and demerits. Chronic use of immunosuppressant has severe adverse effects. This study aimed to compare the efficacy of two immunosuppressants viz prednisolone and cyclosporine in the naturally occurring pemphigus complex cases. Cyclosporine, a calcineurin inhibitor, blocks T-cell infiltration, activation, and the subsequent release of inflammatory cytokines interleukin (IL)-2, IL-4, interferon (IFN)-γ, and tumour necrosis factor (TNF)-α [10,11]. Cyclosporine likely exerts the therapeutic effect in antibody-driven autoimmunity (e.g., pemphigus) by controlling B-cell activation through inhibition of reactive T helper cells interaction with naive B cells [12,13]. The main adverse reactions to cyclosporine therapy are renal dysfunction, hypertension, tremor, hirsutism, and gingival hyperplasia. Low serum magnesium has been reported in some, but not all, patients exhibited convulsions under cyclosporine therapy [14]. Cyclosporine-treated patients showed significant decreases in GFR [15], creatinine clearance, and urea clearance [6], and increases in blood urea nitrogen (BUN) and percent urea reabsorption after intravascular volume depletion [16]. Cyclosporine treated dogs responded favourably with mild gastric discomfort without any changes in the liver and kidney function markers in this study.

Corticosteroids are the most commonly used medications either as a single agent or concurrently with a second immunosuppressive medication. Prednisone or prednisolone at a dose of 2 mg/kg body weight (BW) per day either given once daily or divided into twice daily dosing is the most common medication used. Prednisolone functions through interaction with the cytoplasmic corticosteroid receptor, resulting in upregulation of the expression of anti-inflammatory proteins and downregulation of the expression of pro-inflammatory proteins [17]. The unbound corticosteroid enters cells and exerts its effects by binding to a cytoplasmic corticosteroid receptor, which leads to their translocation into the nucleus and the formation of a dimer that binds to corticosteroid response elements in the promoter region of certain genes [18,19]. In our current study, prednisolone treated dogs though showed faster response in contrast with transient elevation in the blood glucose level and recurrence of clinical signs in few cases. Renal glycosuria, without overt hyperglycaemia, contributed to osmotic diuresis, and GLUT2 downregulation in the proximal tubule may underlie renal glycosuria in cyclosporine administration [20].

Conclusion

Cyclosporine treated dogs responded favourably without much adverse effects as compared to prednisolone treated dogs in the naturally occurring canine pemphigus complex cases.

Acknowledgement

We acknowledge the help extended by animal owners for frequent visit and In charge, RVP for necessary laboratory facilities.

Conflict of Interest

The authors declare that there is no conflict of interest among authors.

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