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The Therapeutic Effects of Prednisolone in Cats with Immune-mediated Hemolytic Anemia

Rosama Pusoonthornthum¹ Parkorn Limlengler¹ Pitcha Pornmingmas²
Anudep Rungsipipat³ Pinit Pusoonthornthum¹

Abstract

The present study was performed to find the therapeutic effects of 2 mg/kg prednisolone orally fed twice a day in cats with immune-mediated hemolytic anemia (IMHA). Six IMHA positive cats were diagnosed with Coomb's test. Mean age of IMHA cats was 4.4 years old. They were considered as having secondary IMHA. The mortality rate of IMHA cats received prednisolone treatment was 33.3%. Complete blood count and blood chemistry values were all within the normal limit.

Keywords: cats, immune-mediated hemolytic anemia, prednisolone

¹Department of Veterinary Medicine, Faculty of Veterinary Science, Chulalongkorn University, Bangkok, Thailand

²Suwannachard Animal Hospital, Bangkok, Thailand

³Department of Veterinary Pathology, Faculty of Veterinary Science, Chulalongkorn University, Bangkok, Thailand.

*Correspondence author E-mail: trosama71@hotmail.com

บทคัดย่อ

ผลการรักษาแมวที่มีภาวะโลหิตจางจากภาวะภูมิคุ้มกันไวเกินด้วยเพรดนิโซโลน

รศมา ภูสุนทรธรรม¹ ภากร ลิ้มเล็งเลิศ¹ พิชา พรหมิงมาศ² อนุเทพ รังสีพิพัฒน์¹ พินิจ ภูสุนทรธรรม¹

ทำการศึกษาผลของการใช้ยาเพรดนิโซโลน ขนาด 2 มก.ต่อ กก. น้ำหนักตัว วันละ 2 ครั้ง ในแมวซึ่งมีภาวะโลหิตจางจากภาวะภูมิคุ้มกันไวเกินด้วยการตรวจด้วย Coomb's Test พบว่า มีแมวป่วยด้วยภาวะโลหิตจางเนื่องจากภูมิคุ้มกันไวเกินจำนวน 6 ตัว ซึ่งมีอายุเฉลี่ยเท่ากับ 4.4 ปี แมวป่วยเหล่านี้เกิดโลหิตจางจากภาวะภูมิคุ้มกันไวเกินแบบทุติยภูมิ แมวป่วยซึ่งได้รับการรักษาด้วยยาเพรดนิโซโลนมีอัตราการตายเท่ากับร้อยละ 33.3 และตรวจไม่พบความผิดปกติของค่าโลหิตวิทยาและเคมีคลินิก

คำสำคัญ: แมว โลหิตจางจากภาวะภูมิคุ้มกันไวเกิน เพรดนิโซโลน

¹ภาควิชาอายุรศาสตร์ คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กรุงเทพฯ

²โรงพยาบาลสัตว์สุวรรณชาติ ถนนสุขุมวิท 3 บางกะปิ กรุงเทพฯ

³ภาควิชาพยาธิวิทยา คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปทุมวัน กรุงเทพฯ

*ผู้รับผิดชอบบทความ E-mail: trosama71@hotmail.com

Introduction

Immune-mediated hemolytic anemia (IMHA) is one of the cause of anemia which red blood cells are destroyed in blood vessels (intravascular hemolysis) and in tissue (extra vascular hemolysis) (Barker, 2000). Prolonged destruction of red blood cells by immunoglobulin and complements results in red blood cell breakdown (Day, 2000; Kohn, 2006^{a,b}). IMHA can cause organs infarction and damage bone marrow leading to a decreased in red blood cells production (non-regenerative anemia) (Weiss, 2008).

Various drugs have been used to treat IMHA in dogs, but there is no standard protocol of treatment for IMHA in cats (Husband et al., 2002). In dogs, azathioprine is commonly used in conjunction with prednisone to treat IMHA (Kucinskiene et al., 2005; Mitchell and Kruth, 2010), but Azathioprine is contraindicated in cats because of its high potential for bone marrow toxicity (Husband, 2002). Other drugs that were used as immunosuppressive agents in cats include cyclosporine, cyclophosphamide, chorambucil, and leflunomide (Gunn-Moore et al., 1999). Cyclophosphamide causes severe side effects including myelosuppression, hemorrhagic cystitis, and gastroenteritis (Dewey et al., 2010). Leflunomide is expensive and there are few reports of its used with IMHA. Chlorambucil is a relatively weak immunosuppressive drug and may not be effective in refractory cases of IMHA and is associated with bone marrow suppression (Dewey et al., 2010). Prednisolone has been used in dogs with IMHA for many years (Grundt and Barton, 2001). Prednisolone causes many side effects including polyuria, polydipsia and an increase in plasma alkaline

phosphatase in dogs but not in cats. The objective of the present study was to test the therapeutic effects of prednisolone orally in cats with immune-mediated hemolytic anemic.

Materials and Methods

Cats with hematocrit (Hct) of less than 27% presented to the Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University and animal hospitals in Bangkok Metropolitan area were studied. Cats with chronic renal failure, blood loss anemia and/or receiving immunosuppressive drug within one month were excluded. IMHA cats were diagnosed by using Direct Agglutination Test (DAT; Coomb's test). Cats with positive Coomb's test were diagnosed with IMHA. The IMHA cats were treated with 2 mg/kg prednisolone orally fed twice a day until the number of red blood cells returned to normal value. Completed blood count (CBC) and blood chemistry (blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT) and alkaline phosphatase (ALP)) were measured. Each IMHA cats was monitored every seven days for the response to prednisolone treatment until the PCV returned to normal. The protocol was approved by Chulalongkorn University Animal Care and Use Committee.

Data analysis: The hematocrit, red blood cell, platelet, white blood cell, ALT, ALP, BUN, creatinine were compared before and after the prednisolone treatment using paired *t*-test. *P*-value of less than 0.05 was considered significant.

Results and Discussion

IMHA was diagnosed in six cats from twenty-five anemic cats with hematocrit of less than 27% (6/25; 24%). These six positive IMHA cats were positive for feline leukemia virus (FeLV; Ab/FeLV Ag Test Kit, Bionote[®]) (3/6), feline immunodeficiency virus (FIV; ^aAnigen Rapid FIV Test Kit, Bionote[®]) (2/6) ^aAnigen Rapid FIV, Bionote[®], and FeLV with feline infectious peritonitis (FIP) positive (1/6). They consisted of one Siamese, one Persian and four domestic short-haired with no gender predisposition. Mean age of cats with IMHA was 4.4 years old. Completed blood count and blood chemistry values of the IMHA cats on the first day of diagnosis are shown in Table 1.

Cat No. 1 was admitted to the hospital for acute hemolytic anemia and had positive autoagglutination. It died on day 4 of the prednisolone treatment. Cat No. 2 presented to the hospital with history of seizure, ear mite and an increased in ALT levels. The owner chose to euthanasia this cat after thirteen days of prednisolone treatment because of the recurrent seizure. Cat No. 4 presented to the hospital with chronic anemia and an increased in ALT levels. Prednisolone was given to this cat, but the clinical sign worsened due to poor client compliance. Cat No. 5 presented to the hospital with acute anorexia, anemic, dyspnea and weakness. He died later of other complications. Cat No. 6 died with acute anemic before the prednisolone was given. Cat No. 3 was presented to the hospital with chronic anemia and response very well to prednisolone treatment. Its RBC increased to normal with the prednisolone treatment. After two months of the prednisolone treatment, the Coomb's test for cat No. 3 was negative. It remained normal for 16 months afterward without any medications.

Primary IMHA is rarely found in cats. Kohn (2006) had reported 19 cats with primary IMHA in Germany (Kohn et al., 2006^a). Cats with IMHA in the present study were positive for FeLV or FIV by ELISA test kit. As in previous studies, IMHA positive cats in this study had secondary IMHA (Day, 1996; Gunn-

Moore et al., 1999). The causes of secondary IMHA may be due to the chronic stimulation by viral infection that increases the amount of circulating immunoglobulin. Non-self antigen from FeLV and FIV infection may also coat red blood cell surface and causes immune system to attack red blood cell resulting in secondary IMHA.

Thrombocytopenia was demonstrated in IMHA positive cats in the present study. The cause of thrombocytopenia may be due to immunoglobulin that damaged platelets number (immune-mediated thrombocytopenia, IMTP) as well as red blood cells. Autoagglutination is negative in five out of six IMHA positive cats. There was a report suggesting that autoagglutination is not a good screening test for feline IMHA due to the low sensitivity. This is contrasted to canine IMHA which often has autoagglutination (Nassiri et al., 2005).

The mortality rate of IMHA cats received prednisolone treatment in the present study was 33.3% higher than one previous study in which the survival rate in 19 primary IMHA cats was 23.57% (Kohn et al., 2006^b). Four of the six IMHA positive cats (4/6, 67%) survive in the present study after receiving the prednisolone treatment. One of the IMHA cats which was positive for FeLV (cat No. 3) and received prednisolone treatment survived from IMHA. Two IMHA cats responded to prednisolone treatment, but IMHA recurred after the owner stopped the drug too soon or the underlying causes of IMHA were not corrected. One IMHA positive cat responded well to the prednisolone treatment and did not relapse. This cat had lymphoma which is one of the causes of the early IMHA. Prednisolone did not cause any side effects in IMHA cats in the present study. None of the treated cats had any changes in ALT levels and no clinical signs suggested the side effects of prednisolone as reported in dogs. Mean total WBC count and blood chemistry profile were within the normal range. In one retrospective study of 19 cats with primary IMHA, 15 of the 19 cats receiving only an immunosuppressive dose of prednisolone experienced an increase in Hct above 25% within 8-42

Table 1 Mean±SEM of blood profile of the IMHA cats on day 0 and day 7 of the treatment

| Parameter | Units | Normal value # | Day 0 (n = 6) | Day 7 (n = 4) |
|-------------|----------------------------|----------------|---------------|----------------|
| RBC | x 10 ⁶ cells/μl | 5.24-10.89 | 2.84±1.25 | 5.85±0.40* |
| Hct | % | 29.2-51.7 | 18.75±0.34 | 33.58±1.27* |
| Platelets | x 10 ⁵ cells/μl | 1.8-2.0 | 0.84±0.46 | ND |
| WBC | cells/μl | 4,200-17,500 | 15,160±8,371 | 12,329±1,639 |
| Neutrophils | cells/μl | 1,925-14,825 | 7,187±959.66 | 5,903±1,244.50 |
| Lymphocytes | cells/ml | 1,100-7,000 | 3,909±916.09 | 2,453±776.64 |
| Eosinophils | cells/μl | 110-750 | 148.2±47.56 | 159.06±95.10 |
| Basophils | cells/μl | 0-190 | 16.87±44.72 | 16.24±46.64 |
| Monocytes | cells/μl | 55-780 | 366.13±116.21 | 365.91±93.26 |
| ALT | IU/l | 28-76 | 45.34±30.11 | 45.57±10.71 |
| ALP | IU/l | 0-62 | 44.85±29.91 | 36.82±6.83 |
| BUN | mg/dl | 15-35 | 22.80±12.16 | 33.11±5.80 |
| Creatinine | mg/dl | < 1.6 | 1.22±0.39 | 1.14±0.31 |

Normal reference value from Sodikoff C.H. 1995. Serum chemical test. Laboratory profile of small animal disease. In: A Guide to Laboratory Diagnosis 2nd (ed). Mosby-Year Book. St. Louis. 3-20.

RBC: Red blood cell, Hct: hematocrit, WBC: White blood cell, ALT: Alanine amino transferase, ALP: Alkaline phosphatase, BUN: Blood urea nitrogen, ND: not determined **p*<0.05

days after starting treatment (Kohn et al., 2006^b). The present study demonstrated that 2 mg/kg prednisolone orally fed twice a day can be used to treat anemic cats with IMHA.

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