HAEMATOLOGICAL AND BIOCHEMICAL EFFECTS OF SULPHADIMIDINE IN NIGERIAN MONGREL DOG

SAGANUWAN, Alhaji Saganuwan
Department of Veterinary Physiology, Pharmacology and Biochemistry, College of Veterinary Medicine, University of Agriculture PMB 2373, Makurdi, Benue State, Nigeria.
Email: PharnSaga2006@yahoo.com Phone: 234 80 27444269

ABSTRACT

Haematological and biochemical effects of sulphadimidine were studied in Nigerian mongrel dogs. Five Nigerian mongrel dogs of either sex weighing between 7 and 12 kg were used for the study. The pretreatment blood and serum samples were collected and the weight of animals taken before the administration of 100 mg/kg body weight for a period of 7 days. The animals were weighed daily. The results showed that there was no significant difference between preadministration and post administration weights (P>0.05) of dogs. Packed cell volume decreased significantly (P < 0.05) with duration sampled dogs. Liver function test revealed significant decrease (P < 0.05) of total bilirubin and alkaline phosphatase. Other indices of liver function and electrolytes indices were normal (P > 0.05). The mean weight gain (8.8 ± 2.04 kg^a) of the animals before sulphadimidine administration was comparable with the weight gain (8.77 ± 0.89 kg^b) of animals after the sulphadimidine administration. Sulphadimidine caused anaemia of moderate value (26.4 ±3.36%^{a}) in the treated samples as compared to pretreated samples (46.4±6.27^b). Total bilirubin (12.32 ±1.4 µmol^a) in pretreatment samples was decreased in comparison with treated (18.5 ±2.0 µmol/l^b) samples. Alkaline phosphatase was decreased in preadministration samples (114.2 ±5.7µg/l^b) as compared to post administration samples (130 ±9.61 µmol/l^a). Therefore longtime administration of sulphadimidine in anaemic mongrel dogs may aggravate anaemic condition. Sulphadimidine may increase renal excretion of bilirubin and decrease bone mineralization in mongrel dogs during bone formation.

Keywords: Haematology, Biochemical effect, Sulphadimidine, Nigerian Mongrel, Dog

INTRODUCTION

The systemic availability of a drug is the amount of administered drug which reaches the systemic circulation intact (Graham-Smith and Aronson, 1992). Measurement of drug concentration in the blood and urine are performed to determine the need for adjustment of the dosage or of the schedule of administration (Saganuwan *et al.*, 2003). Sulphadimidine, a systemic sulphonamide, has maintained an active place in the armamentary of antimicrobial drugs used in veterinary medicine (Saganuwan *et al.*, 2003). It has been proven clinically to be useful for wide range of microbial diseases caused by gram negative and positive bacteria, Nocardia, Actinomyces, Chlamydia, Toxoplasma and Coccidia (Bevil, 1982). Sulphadimidine is 79 % plasma protein bound with half-life of 3.88 to 15.4 hours and has particularly large percentage (60 – 90 %) excreted as acetylated derivatives (Saganuwan *et al.*, 2003). The estimation of bioavailability of sulphadimidine is usually based on the cumulative urinary excretion of the drug (Baggot, 2001).

The protein fractions in the blood are commonly estimated in the serum and do not include fibrinogen that will be precipitated when the blood clots. The main serum proteins are albumin and globulin (Kombo-Owiye and Reid, 1991). The extent of drug binding to plasma proteins varies with the concentrations of drug and plasma protein, the affinity being between drug-binding protein and drug and the number of binding sites per molecule. Within the range of therapeutic concentrations, the extent of drug binding in healthy animals is concentration dependent for some drugs and animal models (Baggot, 2001).

Albumin largely accounts for the binding of acidic drugs such as sulphonamides in plasma. The range of total plasma/serum protein concentration (6.0 - 8.5 g/dl) is similar in domestic animals and humans (Baggot, 2001). Species variation in the binding of acidic drugs may be attributed to differences in the configuration of the plasma albumin that would affect the binding capacity of protein (Baggot, 2001). The aim of the present study was not to establish only normal haematological and biochemical parameters in the healthy dogs but also, to investigate the effects of sulphadimidine on these parameters. The study may serve as a guide to avoiding adverse effects that may be caused by sulphadimidine in Nigerian mongrel dogs as species variation, sex, age, disease condition, environment and nutritional factors sometimes play great role in disposition kinetics of a particular drug.

MATERIAL AND METHODS

Experimental Animals: Five Nigerian mongrel dogs of either sex weighing between 7 and 12 kg were used for this study. The dogs were purchased in Makurdi, Benue State, Nigeria from a dog owner. The dogs were borne the same day and from the same

mother. But they were 6 - 7 months old and fed daily with boiled rice, beans and meat, water was provided adlibitum.

Drug Administrations and Sample Collection: Sulphadimidine was intramuscularly administered at the dose rate of 100 mg/kg body weight into thigh muscles of the 5 dogs daily for a period of 7 days. Prior to administration of sulphadimidine, control blood samples were collected from the dogs: 2 mls of blood was collected from the cephalic vein of each dog into test tubes containing ethylenediamminetetraacetate (EDTA) as anticoagulant for haematological parameters. Another 4 - 5 mls of whole blood was collected from each dog but allowed to coagulate and serum collected for quantitative in vitro determination of biochemical parameters: liver function test and electrolytes determination.

After that, the animals were weighed before sulphadimidine administration and after sulphadimidine administration for 7 days. At the end of 7 days trial, another 1 – 2 mls of blood sample was collected from the cephalic vein of each dog into EDTA bottle and 4 – 5 mls of whole blood was collected from each dog and allowed to coagulate in order to obtain serum for determination of haematological and biochemical parameters respectively. All dogs were weighed.

Determination of Haematological and Biochemical Parameters: Total blood cells count was done using the method of Baker (1985). Total protein was determined using biuret method (Tietz, 1995). Albumin was determined using bromocresol green method (Doumas, 1971). But conjugated bilirubin and total bilirubin were determined using the method of Jendrassik and Grof (1938) whereas Serum Glutamic Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruric Transaminase (SGPT) were determined using the method of Reitman and Frankel (1957). Sodium ion (Na^+) and potassium ion (K^+) were determined using flame photometric method (Fawcett and Scott, 1960). Both bicarbonate (HCO^-_3) and chloride (CL^-) ions were determined using titration method (Chaney and Marbach, 1962).

Statistical Analysis - The data on weight gain or loss, haematological and biochemical parameters were expressed as mean ± S.D. Tests for significance between mean parameters in respect of preadministration and post administration values were performed using student 't' test (Petrie and Watson, 2002).

RESULTS

The mean weight of the animals before administration of sulphadimidine was 8.8 ±2.04 kg[a] whereas the mean weight of the animals post administration of sulphadimidine was 8.77 ± 0.89 kg[b] (P > 0.05) i.e. there was no significant difference between the weight of the animals before and after the treatment with sulphadimidine (Table 1).

Table 1: Effect of intramuscular sulphadimidine on weight gain in Nigerian mongrel dogs

S/No	Control Pre Administration	Experimental Post Administration
1	12.00	10.00
2	7.00	7.86
3	9.00	8.71
4	9.00	9.29
5	7.00	8.0
Mean (kg)	8.80	8.77
Mean ± S.D	8.80 ±2.04	8.77 ± 0.89

Haematology revealed the significant decrease level of packed cell volume (P<0.05). Whereas white blood cells (WBC) neutrophils, lymphocytes, monocytes, eosinophils and basophils levels were not significantly increased (P>0.05) (Table 2).

Table 2: Effects of intramuscular sulphadimidine on haematological parameters of Nigerian mongrel dogs

Indices	Control Pre Administration	Experimental Post Administration
PCV %	46.4 ±6.27[b]	26.4 ±3.36[a]
WBC x 10%	7.54 ±1.45[a]	6.54 ±1.72[b]
Neutrophils %	52 ±7.78[a]	45.40 ±15.96[b]
Lymphocytes%	38.2 ±10.69[a]	44.8 ±8.99[b]
Monocytes%	5.6 ±5.37[a]	4.60 ±2.60[b]
Eosinophils%	4.2 ±2.95[a]	5.20 ±5.63[b]
Basolphils%	0.0 ±0.0[a]	0.0 ±0.0[b]

Keys: *T-test level of significance = 5%, a = Statistically significant, b= Statistically not significant, PCV= Packed cell volume, WBC = White blood cells, N = Neutrophils, L = Lymphocytes, M = Monocytes, E = Eosinophils, B = Basophils*

Liver function test revealed the increase level of total bilirubin and alkaline phosphatase (P<0.05). However, total protein, albumin, conjugated bilirubin, serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) did not increase significantly P>0.05) (Table 3). Electrolytes titration has shown that sodium ion (Na^+) potassium ion (K^+), chloride ion (Cl^-) and bicarbonate ion ($HC0^-_3$) did not increase significantly (P>0.05) (Table 4).

DISCUSSION

The mean weight gain (8.8 ± 2.04 kg[a]) of the animals before sulphadimidine administration is comparable with the weight gain (8.77 ± 0.89 kg[b]) of animals after the sulphadimidine treatment. This shows that sulphadimidine has no effect on weight gain or loss. But the decrease in packed cell volume (P > 0.05) is a clear demonstration of report of Willard *et al* (1989) that in the dog, the severity of the anaemia is arbitrarily indicated by PCV range and that PCV value of 20 – 29 % was moderate. Hence sulphadimidine cause anaemia of moderate value (26.4 ± 3.36 %[a]) in dogs. Although anaemia is the most common erythrocyte disorder that can cause a variety of clinical signs (e.g. weakness, lethargy, heart murmur, pica) or may be sub-clinical and detected only as part of a diagnostic work up (Willard

et al., 1988), the above mentioned signs of anaemia were not noticed before the experiment.

Table 3: Effects of intramuscular sulphadimidine on liver function parameters of Nigerian mongrel dogs

Indices	Control Pre Administration	Experimental Post Administration
TP (g/l)	68.32 ±1.69[a]	68.82 ±2.70[b]
A (g/l)	40.3 ±3.77[a]	38.56 ±3.15[b]
TB (µmol/l)	18.5 ±2.01[b]	12.32 ±1.41[a]
CB (µmol/l)	3.08 ±1.48[a]	2.96 ±0.72[b]
AL (µg/l)	130 ±9.61[b]	114.2 ±5.12[a]
SGOT (µg/l)	20.4 ±11.39[a]	11.0 ±1.41[b]
SGPT (µg/l)	12.0 ±9.4[a]	5.2 ±1.64[b]

Keys: *T-test level of significance = 5%, a = Statistically significant, b = Statistically not significant, TP = Total protein, A = Albumin, TB = Total bilirubin, CB = Conjugated bilirubin, AL = Alkaline phosphatase, SGOT = Serum glutamic oxaloacetic transaminase, SGPT = Serum glutamic pyruvic transaminase*

Table 4: Effects of intramuscular sulphadimidine on electrolytes concentration in Nigerian mongrel dogs

Indices	Control Pre Administration	Experimental Post Administration
Na^+(mmol/l)	135.0 ±1.87[a]	135.2 ±1.92[b]
K^+(mmol/l)	3.58 ±0.19[a]	3.82 ±0.29[b]
CL^-(mmol/l)	100 ±1.87[a]	100.4 ±2.07[b]
HCO^-_3(mmoll)	24.6 ±1.82[a]	25 ±1.58[b]

Keys: *Na^+ = Sodium ion, K^+ = Potassium ion, Cl^- = Chloride ion, HCO^-_3 = Bicarbonate ion.*

The results of liver function test have shown total protein value of 68.32 ± 1.69g/l[a] in Nigerian mongrel dogs. This agrees with the report of Baggot (2001) that the range (60-86 g/l) of total plasma/serum protein concentration is similar in domestic animals and human, but this range was not affected by sulphadimidine administration (P>0.05). However, the total bilirubin decrease (P<0.05) is a clear demonstration of report of Willard *et al* (1989) that decreased bilirubin (12.32 ±1.41 µmol/l[a]) in comparison with (18.5 ±2.01 µmol/l[b]) may be due to drugs that displace bilirubin from albumin. This is further confirmed by Prescott *et al* (2000) that sulphonamides are bound to plasma proteins to an extent varying from 15% to 90%. But there is variation among species in binding of individual sulphonamides.

Moreso, significant difference between preadministration value (130 ± 9.61 µg/l[a]) and post administration value (114.2 ±5.72 µg/l[b]) of alkaline phosphatase may be associated with the injected sulphadimidine which might have inhibited hepatic enzyme. This is supported by Willard *et al* (1979) that bone-origin of serum alkaline phosphatase is commonly increased in animals less than 6 to 8 months old. But in this study sulphadimidine has decreased alkaline phosphatase (P < 0.05).

The decreased level of alkaline phosphatase may affect bone mineralization during bone formation. This is supported by Murray *et al* (2000) that alkaline phosphatase contributes to mineralization but in itself is not sufficient.

Lack of statistical significant difference between preadministration and post administration values (P>0.05) of electrolytes may suggest inability of sulphadimidine to cause sodium (Na^+) potassium (K^+), chloride (Cl^-) and bicarbonate (HCO^{-3}) ions imbalance.

However, the results have shown the normal values of Na^+ (135.0 ± 1.87 mmol/l[a]), K^+(3.58 ± 0.19 mmol/l[a]) and Cl^-(100 ± 1.87 mmol/l[a]) in Nigerian dogs to be lower than those reported: Na^+(141-154 mmol/l), K^+(3.8 - 5.8 mmol/l) and Cl^-(105 – 115 mmol/l) by Willard *et al* (1989) in foreign breed of dogs. Bicarbonate level remains the same in both Nigerian local (24.6 ±1.82 mmol/l[a]) and foreign (17-25 mmol/l) breeds of dogs.

Conclusion: Sulphadimidine did not cause increase weight gain or loss but significantly caused decreased packed cell volume (PCV) as total bilirubin and serum alkaline phosphatase were also significantly decreased. However Na^+, K^+, Cl^- and HCO^-_3 ions were not significantly affected. But the normal values of Na^+, K^+ and Cl^- ions were lower in mongrel dogs as compared to the foreign breed of dogs except that HCO^-_3 level remain the same in both mongrel and foreign breeds of dog.

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