INTERACTION OF SEMDURAMICIN AND SALINOMYCIN WITH CIPROFLOXACIN, ERYTHROMYCIN AND SULPHADIMETHOXIN-TRIMETHOPRIM

K. I. Mahmoud, G. R. El-Sayed* and S. El-Sherbini*

*Department of poultry diseases, *Depatment of Biochemistry and Chemistry of Nutrition*

Faculty Vet. Med., Mansoura university

ABSTRACT

Interactions between each of the ionophores semduramicin (Aviax), salinomycin (Sacox) with each of ciprofloxacin, eryhtromycin and sulphadimethoxin-trimethoprim were investigated. The ionophore under investigation was fed for 28 days to 48-hours baby chicks prior to 7 days medication with each of the previously cited antimicrobial and/or ionophores at recommended levels. Groups of birds contained negative non-medicated controls, ionophore alone, antimicrobial alone and ionophore plus other antimicrobial. Different diagnostic criteria were used. Clinical and toxic signs were detected in groups fed semduramicin and medicated with ciprofloxacin and in groups fed salinomycin and treated with erythromycin. However, spasmodic clonic spasms and incoordination disappeared few hours post appearance. Water consumption was significantly dropped in groups fed semduramicin or salinomycin and supplied with sulfonamides and in groups fed salinomycin and supplied with erythromycin. Reductions in body weight were significantly seen in groups fed salinomycin and supplied with sulphonamides. Relative organ weight of spleen and bursa of Fabricious was not altered by any treatment while the relative liver weight was significantly reduced in groups fed semduramicin and supplied with erythromycin. Biochemically, the aspartate transaminase (AST) level was significantly increased in all medicated groups than in non-medicated negative controls. The uric acid was significantly increased in the groups fed salinomycin and medicated with erythromycin or sulphonamides and in groups fed semduramicin and medicated with sulphonamides. Creatinine phosphoktnase (CPK) level was significantly increased in groups fed semduramicin or salinomycin and in those medicated with erythromycin or sulphonamides and significantly decreased in group fed semduramicin and treated with sulphonamides.

From the data, we recommended that AST, CPK and uric acid should be added to other common tests as diagnostic criteria for drug interaction.

INTRODUCTION

Coccidia is a protozoal parasite that represents a real and permanent menace (threat) to modern intensive poultry production. Increasing mortality, reduction in body-weight, poor feed conversion rate and increasing medication costs are the normal sequelae of intestinal epithelial destruction during coccidiosis.

Ionophores are a polyether anticoccidial compounds that may cause toxicity due to their narrow range of safety and uneven distribution in feed or its incompatibility with other drugs (Dowling, 1992). Undesirable interaction include incoordination, ataxia, leg weakness, diarrhea, reduee water consumption, myocardial enlargement, ascitis, hydropericardium and decreased feed intake and growth rate (Perelman et al., 1986; Reece, 1988, and Dowling, 1992). Salinomycin incompatibility with erythromycin, sulfachlorpyrazine, sulfaquinoxaline, chloramphenicol and tiamulin were reported by Mazlum et al., 1985.

The purpose of the present work is to study the compatibility of semduramycin and salinomycin with ciprofloxacin, erythromycin and sulphadimethoxin-trimethoprim.

MATERIALS AND METHODS

Chickens, housing and diets :

One-day old Hy-line males were obtained and randomly distributed in wire pens with continuous lighting. Feed and water were available ad-libitum. Non-medicated commercial basal diet contained raw protein not less than 21%, crude fat not less than 2.9% and crude fiber not more than 4% as labeled by the producer.

Biochemical studies :

Blood samples were collected when chickens reaches 35 days of age. Sera were separated and stored frozen until their biochemical activities were determined. Serum aspartate transaminase (AST), creatinine phosphokinase (CPK) and uric acid were determined according to the described methods of king (1965), Henery, J. (1974) and Fossatti and Prencipe (1980), respectively.

Statistical analysis :

Data were grouped and expressed as means ± S.D. Group means for body weight, relative organ weight, water consumption and serum biochemical measurements were subjected to analy-

sis of variance (Snedecor and Cochran, 1967) using the general linear models procedure and a software paekage (SAS,1987). Significant differences (determined by analysis of varianee for treatment groups) were compared using Duncan s multiple range procedure (Duncan, 1955). All statements of significance were based on the 0.05 level of probability.

Experimental design :

Compatibility of semduramicin (Aviax, Pfizer Egypt) and salinomycin (Sacox, Hoechst) with ciprofloxacin, erythromycin and sulphadimethoxin-trimethoprim was evaluated using Hay-line males as test animals. The ionophores under investigation were fed for 28 days to the 48-hours baby chicks prior to 7 days medication with each of the previously cited antimicrobial and/or Ionophores were given at recommended levels (25 ppm Semduramicin and 60 ppm Salinomycin). Each treatment (groups) contained 3 replicates of 5 birds/replicate. Groups of birds contained negative non-medieated controls. Ionophores alone, antimicrobial alone and ionophores plus other drugs.

RESULTS & DISCUSSION

Clinically, toxicity was observed in groups fed semduramicin and medicated with ciprofloxacin and in groups fed salinomycin and treated with erythromycin. Toxic signs appeared in some groups in the 2nd day post antibiotic-medication while in the others it appeared in the 3rd or 4th day. Toxicity appears as spasmodic clonie spasms and incoordination that disappeared few hours post appearance.

Water consumption (Table 2) of birds fed ration supplemented with either semduramicin or salinomycin without any antibiotic medication and in those medicated with ciprofloxacin or erythromycin and receiving non-ionophore-treated ration did not differ significantly from negative non-treated control birds. Birds medicated with sulph.-trimethoprim for 7 days following non-Ionophore-treated ration or semduramicin-treated rations showed significant reduction in water consumption in days 1,3,4,5,6 and 7 post-medication; while the drop in those receiving salinomycin-treated ration was significantly evident from day 1 to 7 of sulphonamide medication. Groups fed salinomycin treated ration showed significant reduction in water consumption on day 6 and 7 and on day 5,6 and 7 postmedication with ciprofixacin and erythromycin, respeetively.

Weekly body weight of chickens fed semduramicin or salinomycin from day 2 up to day 35 of age did not show any significant differences from the non-medicated negative controls. Significant reduction in body weight were only seen in groups fed salinomycin and medicated with sulphonamides for 7 days (Table 1).

Relative organ weight (Table 1) of spleen and bursa of Fabricious was not altered by any treatment while relative liver weight was significantly reduced in groups fed salinomicin-treated ration and non medicated via water and in salinomycin-erythromycin group.

Biochemically, the aspartate transaminase (AST) level was significantly increased in all groups fed salinomycin or semduramicin treated ration alone or in those medicated with erythromycin, ciprofloxacin or sulphonamides (Table 3). Groups fed semduramicin-treated ration and medicated with erythromycin represents the most severe AST increase. Uric acid was significantly increased in the groups medicated with ciprofloxacin or sulphonamides, in groups fed salinomycin and medicated with erythromycin, ciprofloxacin or sulphonamides and in groups fed semduramycin and medicated with sulphonamides. Creatinine phosphokinase (CPK) level was significantly increased in groups fed semduramicin or salinomycin and in those medicated with erythromycin or sulphonamides and significantly decreased in group fed semduramicin and treated with sulphonamides.

Chicken toxicity due to interaction of anticoccidial ionophores with other antimicrobial are of great practical interest. The materials tested in the present study were the ionophores salinomycin and semduramicin and the antimicrobial ciprofloxacin, erythromycin, and sulphadimethoxine-trimethoprim.

The known incompatibility of salinomycin and erythromycin (Mazlum et al., 1985) was demonstrated in this trial. it was manifested by appearance of temporary spasms and incordination, reduction in water consumption, decrease relative liver weight and an increase in serum AST and uric acid levels. Salinomycin incompatibility with sulphadimethoxazole-trimethoprim was manifested as significant reduction in body weight, severe drop in daily water consumption and increased serum uric acid and CPK levels. Similar incompatibility of salinomycin and sulfachlorpyrazine and sulfaquinoxaline were reported by Laczay (1988) and Laczay et al., 1989a,b. Ciprofloxacin, a new quinolones, seems to have no delcterious effects on chicken health and performance if given to chicken fed salinomycin medicated ration, except reduction in daily water consumption on day 6 and 7 post- ciprofloxin medication.

Although transient and very fast recovered clinical signs of toxicity (Spasms and incordination) appeared in-groups fed semduramicin treated ration and medicated with ciprofloxacin, non of the heath or biochemical measurements were badly affected.

Incompatability of semduramycin with erythromycin could not be detected except by serum AST elevation and with sulphonamides by elevation of AST, uric acid and CPK serum levels and daily reduction in water consumption .

Table (1) : Effects of ionophores interaction with antimicrobial on body weights and relative organ weights of male Hy-line chickens.

TREATMENTS	BODY WEIGHTS (day 35)	RELATIVE ORGAN WEIGHTS[1]		
		Bursa of Fabricious	Spleen	Liver
Negative controls	199 ± 6.5^{cde}	0.54 ± 0.04^{ab}	0.14 ± 0.03^{b}	4.33 ± 0.05^{bcd}
Ciprofloxacin	217 ± 4.4^{ab}	0.64 ± 0.04^{a}	0.16 ± 0.02^{ab}	4.56 ± 0.17^{abcd}
Erythromycin	221 ± 6.3^{a}	0.55 ± 0.04^{ab}	0.16 ± 0.01^{ab}	5.11 ± 0.14^{a}
Sulphadimethoxazol-trimethoprim	192 ± 6.1^{def}	0.53 ± 0.07^{ab}	0.19 ± 0.02^{a}	4.70 ± 0.27^{abc}
Salinomycin	200 ± 5.3^{bcde}	0.57 ± 0.03^{ab}	0.15 ± 0.01^{b}	3.63 ± 0.16^{ef}
Salinomycin.-Ciprofloxacin	184 ± 7.8^{ef}	0.50 ± 0.02^{b}	0.14 ± 0.01^{b}	4.47 ± 0.23^{bcd}
Salinomycin -erythromycin	187 ± 4.9^{def}	0.59 ± 0.04^{ab}	0.16 ± 0.01^{ab}	3.01 ± 0.12^{f}
Salinomycin- sulphonamides	182 ± 5.2^{f}	0.50 ± 0.02^{b}	0.16 ± 0.01^{ab}	4.62 ± 0.17^{abc}
Semduramycin	204 ± 4.9^{abcd}	0.55 ± 0.05^{ab}	0.16 ± 0.01^{ab}	4.08 ± 0.3^{cde}
Semduramycin-ciprofloxacin	213 ± 4.7^{abc}	0.54 ± 0.05^{ab}	0.14 ± 0.01^{b}	4.50 ± 0.27^{abcd}
Semduramycin-erythromycin	201 ± 7.4^{bcde}	0.57 ± 0.30^{ab}	0.14 ± 0.01^{b}	4.90 ± 0.22^{ab}
Semduramycin-sulphonamides	196 ± 8.8^{cdef}	0.50 ± 0.03^{b}	0.16 ± 0.10^{ab}	3.95 ± 0.17^{de}

1 Values are the mean ± S.D. mean of 3 groups of 5 male Hay-line chickens per group sampled at 35^{th} day of age.
a, b, c,d, e, f Values in a column with different superscripts differ significantly ($P < 0.05$).

Table (2) : Effect of ionophores interaction with antimicrobial on daily water consumption of male Hy-line chickens.

TREATMENTS	DAILY WATER CONSUMPTION (ml/bird)[1]						
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Non medicated Controls	45 ± 1.1^{a}	56 ± 1.2^{a}	60 ± 1.0^{a}	61 ± 3.6^{a}	67 ± 3.3^{a}	97 ± 1.4^{a}	99 ± 1.0^{a}
Ciprofloxacin.	54 ± 0.7^{a}	57 ± 3.1^{a}	58 ± 3.1^{a}	60 ± 5.3^{a}	70 ± 1.1^{a}	87 ± 7.6^{ab}	84 ± 5.8^{ab}
Erythromycin.	49 ± 2.8^{a}	58 ± 2.9^{a}	60 ± 1.1^{a}	66 ± 1.1^{a}	68 ± 1.2^{a}	92 ± 6.2^{ab}	86 ± 14^{ab}
Sulphdimethoxazole-trimethoprim.	51 ± 3.5^{b}	52 ± 3.5^{a}	51 ± 5.2^{b}	34 ± 6.1^{b}	37 ± 2.1^{b}	51 ± 4.8^{cd}	37 ± 2.7^{c}
Salinomycin.	56 ± 1.1^{a}	56 ± 2.0^{a}	61 ± 2^{a}	64 ± 0.9^{a}	69 ± 0.9^{a}	92 ± 8^{ab}	99 ± 0.7^{a}
Salinomycin-ciprofloxacin	52 ± 2.9^{a}	49 ± 2.7^{a}	59 ± 1.3^{a}	60 ± 2.6^{a}	68 ± 1.7^{a}	81 ± 5.4^{b}	80 ± 9.2^{b}
Salinomycin-erythromycin	51 ± 2.3^{a}	54 ± 2.7^{a}	61 ± 2.1^{a}	56 ± 5.2^{ab}	37 ± 5.0^{b}	56 ± 8.1^{c}	48 ± 7.4^{c}
Salinomycin-Sulphatrimethoprim	32 ± 1.5^{b}	34 ± 2.0^{b}	29 ± 0.7^{c}	23 ± 0.7^{c}	29 ± 1.2^{c}	38 ± 2.4^{d}	35 ± 0.7^{c}
Semduramycin	53 ± 2.1^{a}	57 ± 1.7^{a}	59 ± 1.8^{a}	65 ± 1.0^{a}	70 ± 1.0^{a}	99 ± 1.3^{a}	83 ± 6.6^{ab}
Semduramycin-ciprofloxacin.	54 ± 0.9^{a}	58 ± 1.0^{a}	58 ± 2.3^{a}	64 ± 0.9^{a}	71 ± 0.8^{a}	100 ± 0.0^{a}	98 ± 0.0^{a}
Semduramycin–erythromycin.	55 ± 1.1^{a}	56 ± 2.3^{a}	60 ± 1.9^{a}	63 ± 1.1^{a}	70 ± 1.2^{a}	92 ± 4.0^{ab}	85 ± 5.5^{ab}
Semduramycin-sulphatrimethoprim	31 ± 5.8^{b}	47 ± 5.8^{ab}	50 ± 5.8^{b}	35 ± 4.0^{b}	34 ± 5.0^{bc}	45 ± 3.7^{cd}	39 ± 3.7^{c}

1 Values are the mean ± S.D. mean of 3 groups of 5 male Hay-line chickens per group sampled at day1-7 post antibiotic medication.
a,b,c,d Values in a column with different superscripts differ significantly ($P < 0.05$).

Table (3) : Effect of ionophores interaction with antimicrobial on serum biochemical activities of male Hy-line chickens.

TREATMENTS	SERUM BIOCHEMICAL CHANGES[1]		
	AST (U/L)	Uric acid (mg/dL)	CPK (U/L)
Negative controls	298.6 ± 10.3^{c}	5.16 ± 3.1^{c}	6.9 ± 0.3^{de}
Ciprofloxacin	370.3 ± 8.6^{b}	7.90 ± 1.0^{a}	6.8 ± 0.6^{def}
Erythromycin	350.0 ± 2.3^{cb}	6.90 ± 0.8^{abc}	18.6 ± 1.1^{a}
Sulphadimethoxazol-trimethoprim	384.0 ± 2.3^{cb}	$7.8\ 0 \pm 0.9^{a}$	14.1 ± 0.8^{b}
Salinomycin	374.8 ± 9.4^{b}	6.77 ± 0.8^{abc}	9.70 ± 0.5^{c}
Salinomycin.-Ciprofloxacin	363.5 ± 22.8^{b}	8.20 ± 0.5^{a}	8.20 ± 0.3^{cd}
Salinomycin –erythromycin	391.5 ± 34.9^{b}	11.90 ± 0.3^{a}	6.20 ± 0.2^{ef}
Salinomycin- sulphonamides	375.0 ± 10.5^{b}	10.80 ± 0.7^{ab}	17.4 ± 0.8^{b}
Semduramycin	368.5 ± 5.7^{b}	6.90 ± 0.5^{abc}	14.5 ± 0.8^{b}
Semduramycin-ciprofloxacin	369.5 ± 3.4^{b}	5.70 ± 0.3^{bc}	6.30 ± 0.5^{ef}
Semduramycin-erythromycin	468.0 ± 35.5^{a}	6.80 ± 0.2^{abc}	8.70 ± 0.5^{cd}
Semduramycin-sulphonamides	372.0 ± 26.2^{b}	11.1 ± 0.4^{a}	4.9 ± 0.8^{f}

1 Values are the maan ± S.D. mean of 3 groups of 5 male Hay-line chickens per group sampled at 35th day of age.
a,b,c,d,e,f Values in a column with different superscripts differ significantly ($P < 0.05$).

REFERENCES

Dowling, L. (1992) : Ionophore toxicity in chickens: a review of pathology and diagnosis. Avian Pathology, 21:355-368.

Duncan, D. B. (1955) : Multiple range and multiple F tests. Biometrics.11:1-42.

Fossatti, A. and Prencipe, R. (1980) : Enzymatic calorimetric test for determination of uric acid. Clin. Chem. 28:227

Henery, J. (1974) : Creatinine in solution. Clinical Chemistry, principles and techniques. 2nd Ed. Harper and Row, p.525.

King, J. (1965) : Clorimetric method for the activity determination of aspartate aminotransferase and alanine aminotransferase. Practical Clinical Enzymology.Van Nostrand, Co. Ltd. Page 132.

Laczay, P. (1988) : [Compatibility of ionophore antibiotics]. Zur kompatibilat der ionophoren antibiotika. Monatshefte fur Veterindrmedizin, 43:786-788.

Laczay, P.; Simon, F.; Mora, Z. and Lehel, J. (1989a) : [Compatibility of salinomycin and narasin with other chemotherapeutic agents in broilers]. A szalinomicin es a narazin egyeb chemotherapeuticumokkal valo osszeferhetosegenek vizsgalata pecsenyecsirken. Magyar allatorvosok Lapja, 44:173-177.

Laczay, P.; Simon, F.; Mora, Z. and Lehel, J. (1989b) : [Compatibility of some new ionophor anticoccidials with other drugs in broilers]. Zur kompatibilitat der neueren ionophorantikokzidika mit anderen chemotherapeuticumoka bei brollern. Deutsche Tierdztliche Wochenschrift, 96:449-451.

Mazlum, Z.; Pickles, R. W.; Pradella, G., and Pagnani, R. (1985) : Interaction between monensin, narasin or salinomycin and the antibiotics erythromycin, chloramphenicol or tylosin in broiler chicks. Clinical Veterinaria, 108:95-104.

Perelman, B.; Abarbanel, J. M.; Gur-Lavie, A.; Meller, Y., and Elad, T. (1986) : Clinical and pathological changes caused by the interaction of Lasalocid and chloramphenicol in broiler chickens. Avian Pathology, 15:279-288.

Reece, R. L. (1988) : Review of adverse effects of chemotherapeutic agents in poultry. World s Poultry Science Journal, 44:193-216.

SAS "Statistical Analysis System" (1987) : SAS Institute, Inc. SAS user guide: Statistics. SAS Institute, Cary, N.C. 1987. a Microcomputer version 6.03.

Snedecor, G. W. and Cochran, W. E. (1967) : Statistical methods. 6th ed. Iowa state university Press., Ames, Iowa.

الملخص العربى

تفاعل مضادات الكوكسيديا (السيمديوراميسين والسالينوميسين) مع السبروفلوكساسين، الأرثروميسين والسلفا داى ميثوكسين - ترای ميثوبريم

كامل إبراهيم أبوالعزم جهاد رمضان السيد* السعيد الشربينى السعيد*

قسم أمراض الدواجن والأرانب - قسم الكيميا ، الحيوية وكيميا ، التغذية*

كلية الطب البيطرى - جامعة المنصورة

فى هذا البحث تم دراسة التفاعلات الناتجة عن تغذية الدواجن على علائق بها مضادات كوكسيديا (سيمديوراميسين، سالينوميسين) والعلاج بالسبروفلوكساسين، إرثروميسين، السلفا داى ميثوكسين، ترای ميثوبريم وقد ظهر على الطيور تشنجات وعدم القدرة على الحركة.

فى مجاميع السيمديوراميسين - سبروفلوكساسين ومجموعات السالينوميسين - إرثروميسين ظهرت الأعراض فى بعض المجاميع فى اليوم الثانى فى حين ظهرت فى مجاميع أخرى فى اليوم الثالث والرابع من بداية إعطاء مضادات البكتريا سالبة الذكر ولم تستمر الأعراض سوى لبضع ساعات.

إنخفض معدل الإستهلاك اليومى للمياه فى المجاميع المعالجة بمركب السلفا والمغذاه على أعلاف بها سيمديوراميسين أو سالينوميسين وكذلك فى مجموعة الأرثروميسين - سالينوميسين كما إنخفض وزن الطيور فى المجاميع المعالجة بالأرثروميسين والمغذاة على أعلاف بها سالينوميسين.

لم يتأثر الوزن النسبى للطحال وغدة فبريشى بأى من المعاملات سالفة الذكر فى حين إنخفض الوزن النسبى للكبد فى المجموعة المعالجة بالأرثروميسين أثناء تواجد السالينوميسين فى الأعلاف.

أظهرت النتائج البيوكيميائية زيادة فى إنزيم كفاءة الكبد (الإسبرتات ترانس أمينيز) فى كل المجموعات المعالجة عن المجموعة الضابطة، كما حدثت زيادة فى حامض البوليك فى المجموعات المغذاه على السالينوميسين والمعالجة بالآرثرومبسين أو مركبات السلفا، وكذلك فى المجموعة المغذاه بالسيميديوواميسين والمعالجة بمركبات السلفا، كما حدثت زيادة معنوية فى إنزيم الكرياتينين فوسفوكينيز فى المجموعات المغذاه على السيميديوراميسين أو السالينوميسين والمعالجة على مركبات الأريثروميثين أو السلفا، وحدث إنخفاض معنوى فى هذا الإنزيم فى الطيور المعالجة بالسيميديواميسين والمعالجة بمركبات السلفا.

فى هذه النتائج نستخلص أنه يمكن الإستعانة بنسبة الإسبرتات ترانس أمينيز وحامض البوليك والكرياتينين فوسفوكينيز كتحليلات معملية لتشخيص التداخلات الدوائية التى تحدث فى مجال الدواجن.