COMPARATIVE EFFICACY OF CEFTIOFUR SODIUM (EXCENEL)^{R} AND KANAMYCIN IN TREATMENT OF PNEUMONIA IN BUFFALO-CALVES

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ABSTRACT

The present study was carried out using 60 buffalo-calves aged 6-9 months, 30calves were clinicaly normal and divided into three groups. The first group was kept as control (healthy untreated) the second group received therapeutic dose of ceftiofur sodium for 5 succussive days and the third group received therapeutic dose of Kanamycin for 5 succussive days. The rest 30calves showed the clinical signs of pneumonia were randomaly divided into three groups, the first was kept as control (infected untreated), the second was received therapeutic dose of ceftiofur sodium for 5 succussive days, third group infected and received therapeutic dose of Kanamycin for 5 succussive days.Clinicopathological and bacteriological furtheremore efficacy of ceftiofur sodium and kanamycin in treatment of pneumonia were recorded. Bacteriological findings indicated that E. coli, pasteurella multocida, strept. Pyogen, staph. aureus, klebaiella pneumonae and mixed infection (E. Coli and pasteurella multocida) in precentage of 20%, 30% ,13.3%, 16.7%, 10% and 10% respectively.The antibiogram studies reveald that ceftiofur sodium and kanamycin were the most effective antibacterials against most bacteria isolated from pneumonic calve. Significant elevation in the transaminase enzymes (AST and ALT) glucose, urea and creatinine were observed in pneumonic calve while alkaline phosphatase insignificant increase, hypoproteinaemia, hypoalbuminaemia hypoglobulinemia hypocalcaemia hyponatrim, hyperglycemia and elevation in urea and creatinine levels were noticed. All above mentioned parameters were retuerned to the normal after medication stopping Efficacy of ceftiofur sodium in vivo study when compared with kanamycin was found to be highly effective for treatment of pneumonia, the cure rate was (80% while kanamycin was 66.6%).

INTRODUCTION

Pneumonia is a major problem in buffalo – calves it represents the most important cause of calve mortality that leads to sever economic losses (**Abd-El Ghani *et al.*, 1990 and Musser *et al.*, 1996**). The harmful impact of the

disease is effected through impairment of liver and kidney functions (**Amany, 1997**). Biochemical alterations in pneumonic calves were reported by **Youssef *et al.*, (1990)**. The outbreaks of respiratory disorders among buffalo – calves may be attributed to pasteurlla multocida, pasteurlla. haemolytica and corynbacterium pyogenes (**EL-Allaway *et al.*, 1979**) as well as Staph. aureus, Strept. pyogenes and E. coli (**Elyes, 1982**). Buffaloes have sort of resistance against infection compared with other domestic live stock (**Shalash, 1984**).

Ceftiofur sodium is a third generation of cephalosporins antibitotics, showed a broad spectrum activity (**Brander *et al.*, 1982**). It is bactericidal destroying bacteria by preventing the synthesis of the cell wall (**Yancey *et al.*, 1987**). It is effective than other cephalosprins against many bacterial infection but it is highly effective against pasteurlla species (**Alms, 1988**).

Kanamycin is an aminoglycositd and isolated in Japan from streptomyces kanamyceticus (**Umezawa *et al.*, 1957**). Clinically used extensively to treat bacterial infections in feverish patients (**Prescott and Baggot, 1993**).

The present work was carried out to investigate some biochemical alterations associated with pneumonia in buffalo-calves as well as to evaluate the efficacy of ceftiofur sodium and kanamycin for controlling the pneumonia and reducing the risk.

MATERIAL AND METHODS

Animals:

This study was carried out in a private farm at Hehia (El-Sharkia – Governorate) during the period from September 2000 to January 2001. A total number of 60 buffalo – calves aged from 6-9 months were involved in this investigation. The animals were classified into two groups 30 each.

- The first group was clinically healthy and divided into 3 subgroup 10 each.
- first subgroup healthy untreated (Healthy control)
- second sub group healthy animal injected with therapeutic dose of ceftiofur sodium 1mg/kg B.W. for 5 succussire days (I.M.).
- third subgroup healthy animal injected with therapeutic dose of kanamy cin 5 mg/kg B.W. for 5 succussive days (I.M.).
- second group pneumonic animals and suffering from signs of respiratory troubles including bilateral nasal discharge, cough, fever, congested mucous membranes, lacrimation, abnormal lung sounds. This group was divided into three subgroups 10 each.
- first subgroup pneumonic untreatment (infected untreated control).
- second subgroup pneumonic animal and treated with therapeutic dose (1mg/kg b.w.) of ceftiofur sodium for 5 succussive days (I.M.).
- third subgroup pneumonic animal and treated with therapeutic does (5 mg/kg b.w.) of kanamycin for 5 succussive days (I.M.).

Drugs:

1) Ceftiofur sodium (excenel)^{R} a vial containing 1-4 gm. Was obtained from Upjohn Co. kalamazoo, U.S.A.
2) Kanamycin, a bottle containing 100 ml (each 1 ml contain 100 mg Kanamycin) manifactured by Egyp. Comp. For Chem. and Pharm. (Adwia) S. A. E. 10th of Ramadan city (El-Sharkia – Governorate).

Bacterial examination:

Sterilized swabs were tacken from nasopharynal of apparently healthy and diseased calves for bacteriological examination. The collected samples were incubated in nutrient broth at 37^{0} C for 24 h., then subcltured into selective media according to (**Woldehiwet *et al.*, 1990**). All bacterial isolates were identified after **Holt *et al.*, (1994)**.

Biochemical examination:

From healthy and pneumonic calves blood sample were collected in centrifuge tube via Jugular vien puncture after 7 and 14 days from the medication to obtaining clear serum to be used for measuring the activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) according to **Reitman and Frankel, (1957)**, alkaline phosphatase according to (**John, 1982**). Serum glucose was determined after **Trinder (1969)**, serum total proteins (**Doumos, 1974**) serum albumin (**Drupt, 1974**) and serum globulin was calculated as difference between total proteins and albumin. Serum urea was estimated according to **Fawcet and Scott, (1960)** and serum creatinine (**Husdan and Raporpot, 1968**). Serum calcium was determined according to **Gindler and King, (1972)** and serum sodium (**Henry *et al.*, 1974**).

Antibiotic sensitivity:

The in vitro antibiotic sensitivity test of different isolated microorganism against antibacterial agents was carried out using disc method described by Goald and Bowie (1952). The used antibiotic are ceftoifur sodium (10ug) kanamycin (30 ug) erythromycin (15 ug) spectinomycin (10 ug) flumequine (30ug) and enrofloxacine (10ug).

Treatment trials:

Two groups of pneumonic calves were treated with either ceftiofur sodium (1mg/Kg B.W.) or kanamycin (5mg / kg. B.W.) intramuscular route from the respective drug for 5 consecutive days.

Statistical analysis:

The obtained data were statistically analyzed according to **Snedecor and Cochran, (1976).**

RESULTS

A) Bacteriological isolation:

Bacteriological examination of the culture swabs from 30 pneumonic animals revealed that the isolated bacterial pathogens were Pasteurella multocida (9cases) 30%, E. coli (6cases) 20%, Staph. aureus (5cases) 16.70%, Strept pyogens (4cases) 13.3%, Kelbsiella pneumonae (3cases) 10% and mixed infections including (Pasteurella multocida and E.coli) 3 casess 10%.

B) Antibacterial sensitivity tests:

Table (1) revealed that the isolated strains showed a highest sensitivity to ceftiofur sodium in vitro, followed by kanamycin, enrofloxacine and spectinomycin respectively, and the least sensitivity was found against erythromycin.

C) Biochemical Investigations:

Pneumonic calves showed elevated in transaminases (AST, ALT) activities alkaline phosphatase, glucose, urea and creatinine conceneration but showed significant decrease in total protein, albumin, globulin, calcium and sodium, conceneration on other hand biochemical, parameters returned to the normal levels 15days following treatment Table (2).

D) Anti-bacterial in vivo "Efficacy":

Improvement of clinical symptoms was observed following administration of ceftiofur sodium and Kanamycin. It was found that treatment with ceftiofur sodium was the beter than treatment with kanamycin because the total cure rate of ceftiofur sodium was 80% while that of kanamycin was 66.6% Table (3).

DISCUSSION

Continous research for new drugs for controlling the disease is necessity ceftiofur sodium a broad spectrum beta – lactamase resistant cephalosporin (**Yancey *et al.*, 1987**). Kanamycin has bactericidal antibiotic which affect protein synthesis and alters permeability of the bacterial cell membrane.

The obtained results in our study revealed that E.coli, Pasteurlla multocida, Staph. aureus, Strept pyogens, Kelbsiella pneumonae and mixed infection (E. coli + Pasteurlla multocida) in percentage of 20% , 30% , 16.7% , 13.3% 10% and 10% respectively were the main caustive organsims that responsible for pneumonia in tested animals. These findings were similar to that reported by **El-Sheikh *et al.*, (1994); Mosier, (1997); Mokhbatly and Selim, (1999) and Taha, (1999)**.

Pneumonia induce significant increase in transaminases (AST and ALT) activities but serum alkaline phosphatase did not show any chang in our results in the tested calves could be attributed to the degenerative and necrotic changes accompanied the damage of pulmonary tissue due to bacterial infection and its toxins (**Attia and Essa, 1997 and Kaneko, 1989**). Our results agree with that of **Saleh and El-Bably, (1998) and Mokhbatly and Selim, (1999)**. They found significant increase in AST and ALT activities in buffalo – calves suffering from pneumonia. **El-Sherbini *et al.*, (1996)** reported that pneumonia did not induce any change in alkaline phosphatase activities in pneumonic buffalo-calves.

Concentrations of total proteins, albumin and globulin in the calves suffering from pneumonia in our obtained results (table2) were evident to show significant decrease in comparison with apparently healthy calves. The above mentioned results were supported by previous studies (**El-Naggar 1979; Youssef *et al.*, 1990 and Veysi *et al.*, 1993**). These results could be attributed to the state of aneroxia and inability of the proteins synthesis. Moreover, bacterial toxins increased the capillary permeability and permitted escape of plasma proteins into tissue resulting in hypoproteinemia (**Doxey 1971; Selim, *et al.*, 1977 and Naser and El Saed, 1997**). These results seem to agree with those reported by **Cornelius, (1960)**, who considered febrile diseases to be the most common reasons for hypoproteinaemia and hypoalbuminaemia. Same findings were detected in human by **Chanutin and Gjessing, (1946)**.

There were no significant differences in the liver enzymes (AST, ALT and Alkaline phosphatase) total proteins, albumine and globuline between the normal buffalo – calves given ceftiofur sodium kanamycin and the normal ones that were given no medication which agree with **Abd-Latif and Gamal El-Din, (1998)**, who found that the normal chickens given ceftiofur sodium showed no significant difference in liver enzymes, total proteins but increase in AST compared to control. Same results were reported by **Shalaby and Amer, (1990) and Gammaz and Abd-Alla, (1991)** they found that netilmicine induced non significant effect on AST, ALT, total proteins in rats injected with therapeutic dose.

In the present investingation a significant increase in glucose level in pneumonic calves were observed. These results coincided with those obtained by **El Sayed *et al.*, (1992); Saleh and El-Bably, (1998); Mokhbatly and Selim, (1999) and Taha, (1999)**. **Coles, (1986)** attributed the cause of hyperglycaemia to aneroxia liver glycogen is unstable in the presence of deficient oxygen supply in preumonic calves.

Pneumonic calves showed significant increase in serum urea and creatinine. This increase may be attributed to increase protein catabolism and decreased renal blood flow which might occur in cases of pneumonia which tend to increase urea and creatinine levels (**Radostilis *et al.*, 1995 and Atlia**

and Essa, 1997). Our results were similar to those previously recorded by **El-Sheikh *et al.*, (1994)**.

Normal buffalo – calve given ceftiofur sodium showed no significant diffrence in glucose, urea and creatinine but kanamycin induce significant decrease in glucose, creatinine and increase in urea after 7 days as compared with normal untreated calves which agree with reported by **Abd-Latif and Gamal El-Din, (1998)**, where they mentioned that adminisitration of therapeutic dose of ceftiofur sodium to normal chicken induce non significance chang in urea and creatinine.

Aminoglycoside antibiotic induce nephrotoxicity and increase in urea **Bennet *et al.*, (1977); Shalaby and Amer, (1990) and Gammaz and Abd-Alla, (1991)**, where they mentioned that administration of therapeutic doses of netilimicine to normal rats induce significant decrease in glucose, urea and creatinine. Kanamycin the least nephrotoxic aminogly coside (**Appel and Neu, 1977**).

Serum electrolytes levels including calcium and sodium were significantly decreased in pneumonic-calves. Our results were inagreement with those obtained by **Taha, (1999) and Osama *et al.*, (2000)**.

Healthy calve treated with ceftiofur sodium showed significant decrease in calcium. These results reinforced the findings of **Amer and Abd El-Alim, (2000)**, they reported that ceftiofur sodium treatment resulting in disturbace of the electrolyte balance mainfested by decrease of calcium. This finding might be attributed to disturbance in electrolyte absorption, distribution, metabolism and elemination due to the effect of ceftiofur sodium in G.I.T., liver and kidney (**El-Atar *et al.*, 1997**). kanamycin induced significant increase in calcium and sodium in healthy calve treated with kanamycin in therapeutic doses , same results recorded by **Luft *et al.*, (1978)**.

In vitro sensitivity tests indicated that isolated strains showed highest sensitivity to ceftiofur sodium and kanamycin , the obtained results were consistent with those of **Yancey *et al.*, (1987); Salmon *et al.*, (1996) and El-Sayed *et al.*, (2000)** They concluded that ceftiofur sodium is highly active against Pasteurlla spp but **Watts *et al.*, (1993)**, found that the ceftiofur sodium was the most active against E.coli and Salmonella spp. **Dinh and Ngugen, (1995)** reported that kanamycin was the most effective against isolated E.coli.

Treatment of pneumonic calve with either ceftiofur sodium or kanamycin with the previously mentioned doses revealed that the cure rate was 80% and 66.6% respectively. These results reveald that ceftiofur sodium effective in case of infection with E. coli (100%) Pasteurlla multocida (100%) Staph. auraeus (50%) and Strept pyogens (50%) this finding was similar to that reported by **Yancey *et al.*, (1987); Alms, (1988) and Saman *et al.*, (1990)** they reported a good efficacy of ceftiofur sodium against pasteurlla species, Ecoli and staph. aureus. Moreover , **Bown *et al.*, (1991)** found that

ceftiofur sodium had a wide spectrum of anti bacterial activity against both G +ve and G -ve bacteria including anaerobic bacteria. Kanamycin is very suitable for treatment of serverG-ve bacterial infection as E. coli (**Eichenwald, 1966**).

Recovery from the disease was confirmed through the recorded after treatment with ceftiofur sodium, kanamycin and the measured parameters returned to normal levels.

It could be concluded that ceftiofur sodium has a good efficacy in treatment of pneumonia in buffalo–calves than kanamycin.

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Table (1): Sensitivity test of isolated organisms against different antimicrobial agent.

Antibiotic Discs	Disc concentration	E. Coli	Pasteurlla multoicda	Staph. aureus	Strep. pyogens	Kelbsiella Pneu.	Mixed infection
Cftiofur sodium	10 ug	+ ++	+++	+++	++	-	+++
Kanamycin	30 ug	+++	+	+++	++	+++	++
Spectinomycin	15ug	++	++	++	+	-	+
Flumequine	30 ug	++	+	+	+	+	+
Enrofloxacin	10 ug	++	+++	++	+	+	++
Erythromycin	15 ug	-	+	++	++	+	-

Table (3): Efficacy of treatment with ceftiofur sodium (1 mg / kg b.w.), Kanamycin (5mg / kg b.w.) administered intramuscuarly daily for five consecutive days to buffalo-calve suffering from pneumonia.

Isolated bacterial Treatment	Total number	E. coli			p. multocida			Staph. aureus			Strep. Pyogen			Kelbsiella pnau.			Mixed infection			Total cure Percent	
		T.N .T	Respond cases N.	%.	T.N .T	Respond cases N.	%	T.N .T	Respond cases N.	%	T.N .T	Respond cases N.	%	T.N .T	Respond cases N.	%	T.N.T	Respond cases N.	%	N.	%
Ceftiofur sodium	15	3	3	100%	5	5	100%	2	1	50%	2	1	50%	1	-	-	2	2	100%	12	80%
Kanamycin	15	3	3	100%	4	1	25%	3	3	100%	2	1	50%	2	2	100%	1	-	-	10	66.6%

T.N.T. = total number treated.

Table (2): Effect of ceftiofur sodium (1 mg / kg b.w.), Kanamycin (5mg / kg b.w.) on some serum constituents of healthy and pneumonic buffalo-calve after intramuscular injection for 5 consecutive days at 7 and 14 days post injection (n = 10 calves).

groups / parameters	Unite	Healthy animals					Diseased animals				
		untreated (control)	treated				untreated pneumonic	treated			
			Ceftiofur sodium		Kanamycin			Ceftiofur sodium		Kanamycin	
			7	14	7	14		7	14	7	14
A S T	U/L.	32.18 ± 1.002	33.47 ±0.92	34.08 ± 1.51	35.40 ± 1.90	35.44 ± 1.75	*** 36.96 ± 0.37	* 35.04 ± 0.42	32.27 ± 0.65	* 34.86 ± 0.65	34.49 ± 1.31
A L T	U/L.	11.42 ± 1.08	11.91 ±0.95	13.41 ± 1.87	12.19 ± 2.15	14.76 ± 1.22	** 16.12 ± 1.13	* 14.58 ± 0.38	12.77 ± 0.99	* 14.49 ± 0.63	12.57 ± 0.54
Alk. Ph.	Mg/dl	12.92± 0.77	12.73 ±1.31	13.73 ±1.32	11.35 ±0.95	13.20 ±1.15	13.65 ±0.98	14.16 ± 1.37	12.86 ± 1.40	13.21 ± 1.50	12.53 ± 1.18
T.P.	gm/dl	9.66 ± 0.70	8.65 ±0.44	9.32 ±0.93	8.90 ±0.37	9.20 ±0.55	** 7.00 ±0.41	7.98 ±0.42	8.96 ±0.66	7.98 ± 0.70	10.35± 0.87
albumine	gm/dl	5.76± 0.47	5.62 ±0.46	6.10 ± 1.20	4.96 ± 0.55	5.70 ± 0.33	* 4.00 ± 0.32	4.69 ± 0.38	5.34 ± 0.48	4.28 ± 0.40	5.73 ± 0.44
globulin	gm/dl	3.90 ± 0.22	3.03 ±0.23	3.22 ± 0.25	3.94 ± 0.19	3.40 ± 0.52	** 3.01 ± 0.20	3.29 ± 0.32	3.62 ± 0.32	3.70 ± 0.14	4.62 ± 0.24
glucose	mg/dl	65.99± 3.03	62.32 ± 1.85	63 ±2.53	* 56.52 ± 2.34	64.11 ± 2.15	** 78.96 ± 2.18	70.66 ± 2.93	66.83 ± 2.59	67.21 ± 3.15	63.20 ± 2.95
Urea	mg/dl	37.52 ± 1.55	37.92 ±1.61	37.60 ± 1.90	* 41.24 ± 0.78	40.34 ±0.84	** 42.22 ±0.63	38.77 ± 1.05	37.59 ± 0.72	* 41.40 ± 0.43	39.80 ± 0.35
Creatinine	mg/dl	1.53 ± 0.22	1.73 ± 1.9	1.61 ± 0.45	* 0.96 ± 0.10	1.88 ± 0.06	* 2.14 ± 0.15	1.83 ± 0.20	1.66 ± 0.20	* 2.02 ± 0.03	1.86 ± 0.08
Calcium	mg/dl	10.6 ± 1.2	* 6.8 ± 1.3	9.2 ± 1.4	* 14.3 ± 1.2	12.4 ± 1.7	* 7.0 ± 1.2	9.8 ± 1.5	9.9 ± 1.2	9.7 ± 1.3	11.3 ± 1.1
Sodium	Meq/l	130.5 ± 1.5	134.5 ±2.1	133.4 ± 1.9	** 139.1 ± 1.7	135.3 ± 2.4	** 123.3 ± 1.2	129.5 ± 1.35	132.3 ± 1.91	127.7 ± 1.9	129.5 ± 1.5

*** Significant at P < 0.05** *** * Significant at P < 0.01** ***** Significant at P < 0.001**

الملخص العربي

مقارنة كفاءة السفيتى فيورصوديوم (الأكسنيل) و الكانامسين في علاج الالتهاب الرئوي في العجول الجاموس

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تم إجراء هذه الدراسة على ٦٠ عجل جاموس عمر ٦-٩ شهر منهم ٣٠ بصحة جيدة وأخرى مريضة بالالتهاب الرئوي . قسمت هذه العجول السليمة إلي مجموعة سليمة ولم تعالج (محكمة) والثانية والثالثة سليمة وتم حقنها بالجرعة العلاجية لمدة خمس أيام من السفتى فيور صوديوم والكانامايسين علي التوالي والثلاثون الأخرى مصابه بالالتهاب الرئوي حيث قسمت إلي.مجموعة مصابة ولم تعالج (محكمة مصابه) والثانية والثالثة مصابة وتعالج بالسفيتىفيورصوديوم والكانامايسين بالجرعة العلاجية علي التوالي لمدة خمس أيام متتالية .

وقد تم عزل الميكروبات القولوني العصوي، باستريلاملتوسيدا، السبحى الصديدى ، العنقودى الأبيض ، كلبسيلا نومنى وعدوى مشتركة (الميكروب العصوي مع باستريلاملتوسيدا) بنسب ٢٠%، ٣٠%، ١٣,٣% ،١٦,٧% ،١٠% ،١٠%علي التوالي وبعمل اختبار الحساسية لهذه العترات وجد أن السفتي فيور صوديوم ، الكانامايسين ، الانروفلوكساسين اكثر المضادات الحيوية تأثيرا علي هذه العترات.

الالتهاب الرئوي أدى إلي زيادة معنوية في نشاط الامينوترنزفيراسس وزيادة غير معنوية في نشاط الفوسفاتيز القاعدي. كما أدى إلي نقص معنوي في البروتين الكلي ، الزلال الجلوبيولين ، الكالسيوم والصوديوم كما أدى إلي زيادة معنوية في مستوى الجليكوز في السيرمالسيروريا والكرياتينين . كما تلاحظ أن استخدام السفتى فيور صوديوم والكانامايسين أديا إلي عودة هذه الوظائف إلي المستوى الطبيعي في فصل العجول المصابة والمعالجة .

بدراسة كفاءة السفتى فيور صوديوم والكانامايسين في علاج الالتهاب الرئوي وجد أن السفتى فيور صوديوم له تأثير أقوى من الكانامايسين بنسبة شفاء ٨٠ والكانامايسين ٦٦,٦%.