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EFFECT OF CEFQUINOME IN TREATMENT OF DIARRHEA IN CALVES

El-Sayed, M. G.*, Mohamed El-Diastyand Doaa M. Waheed**

**Department of Pharmacology Faculty of Vet. Med. Mansoura University. Egypt*
*** Animal Health Research Institute. Mansoura. Egypt*

ABSTRACT

This study was conducted by using cefquinome for the treatment of diarrheic calves. 20 diarrheic Holstein calves (3- 15 day old) were used and divided into 2 groups (10 animal / group). The first group was injected intramuscularly by cefquinome (2mg/kg body weight). The second group was served as control . Results revealed a significant increase on total leucocytic count, globulin, aspartate transaminase (AST), Alkaline phosphatase (ALP), urea and creatinine. On the other hand there were a significant decrease in total erythrocytic count, hemoglobin content, packed cell volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, neutrophil count, thrombocyte count, total protein and albumin in cefquinome treated group compared to the control one.

INTRODUCTION

Calf diarrhea is a multifactorial disease entity that can have a serious financial and animal welfare implications in both dairy and beef sucker herds. It has been estimated that 75% of early calf mortality in dairy herds is due to acute diarrhea in the pre-weaning period and also, acommonly reported disease in young animal and still amajor cause of productivity and economic loss to cattle producers and also a cause of high morbidity and mortality in the cattle industry world wide ***(Acress et al, 1977, Quigiey et al., 1995, Wells et al., 1996, Uhde et al., 2008 and Bartels et al., 2010)***. Neonatal calf diarrhea (NCD), mostly occur in calves aged one month-old or younger is a complex disease that can be triggered by both infectious and non-infectious causes **(Bartels et al., 2010 and Windyer et al., 2014).**

Enterotoxigenic E.coli (ETEC) is the most common cause of diarrhea in calves but more recently;attaching and effacing *E.coli*(AEEC) and Shigatoxin-producing *E.Coli* (STEC) have also been identified as a cause of diarrhea and dysentery in calves. Enterotoxigenic E.coli strain (ETEC) is producing the K99 (F5) adhesion antigen and heat-stable enterotoxin and following ingestion, ETEC infects the gut epithelium and multiplies in enterocytes of intestinal villi. The bacteria express the K99 antigen for the attachment. As the fimbrial adhesion F5(K99) promotes the attachment to f bacterial cells to glycoproteins on the surface of epithelial cells of the jejunum or ileum. The bacterial entertoxins also cause damage to epithelial cells, resulting in fluid secretion and diarrhea. Most calves are affected in the first 3 days of life and develop watery diarrhea. The infection with E.coli is considerd as a clinical disease due to E.coli in calves the septicemic illness, being one of the most important causes of neonatal mortility in dairy calves. ***(Acres,1985, Francis et al., 1989, Mainil et al., 1993, Nataro and Kaper, 1998, Lofstedt et al., 1999,***

Frydendahl,2002, Kaper et al., 2004, Foster and Smith, 2009).

Cefquinome Sulfate (CS) is a fourth-generation cephalosporin antibiotic, which has been developed only for veterinary use. It shows potent antibacterial activity against a broad spectrum bacterial species, such as a large number of Gram–positive bacterium. Some of Gram–negative bacterium, vibrios, spirochete, mycoplasma**.** It is an aminothiazolyl cephalospoin, it has, stability against b-lactamase as it is resistant to b-lactamases produced by majority of pathogenic bacteria*. (Coulthurst et al., 2005).*

CFQ is effectively used as therapy of acute diarrhea sustained by *Escherichia coli* as the experimental animals infected with E.coli recovered better after intramuscular cefquinome treatment (2mg/kg). **(*Dumka et al., 2013).***

This research was planned to diagnose and differentiate different causes of scour in calves and also to evaluate some pharmacological effects of cefquinome on blood picture, liver and kidney functions and body weight in calves.

MATERIAL AND METHODS

1. Drugs:

Product name: Cobactan 2.5% injection.

Company: Cefquinome was obtained from MSD animal house, USA.

Description: A bottle (50 ml) of sterile suspension solution for injection each 1ml of the suspension contains 29.64 mg cefquinome sulphate (equivalent to 25 mg cefquinome).

Dose: 2mg /kg body weight for 3 successive days **(Ehinger *et al.,* 2006)**.

2. Experimental calves:

Ten diarrheic Holstein calves (3-15 days old) infected with E. coli in a special dairy farm at Damietta Governorate and injected intramuscularly in the thigh muscle by cefquinome (2mg/ kg body weight) for 3 successive days and other ten healthy calves were kept as a control group. Calves under our experiment were determined after long period of survey (12/2014 – 7/2017) in different dairy farms at Dakahlia and Damietta Governorates; our survey was done on 150 diarrheic calves at different seasons at 3-20 days old age.

3. Kits for diagnosis:

Kits were obtained from BIONOTE Company, Korea.

4. Sampling

Two blood samples (the first one used for hematological studies and the second one used for serological studies) were collected from each animal at zero day, 3rd, 7th and 14th day according to **Stoffregen et al. (1997).**

5. Hematological studies:

Were carried out using fully Automated cell counter (mindary BC-2800).

6. Serum Biochemical Analysis:

(A) Liver function tests:

- **Determination of Total Protein level** according to **Doumas, (1975)**.
- **Determination of Albumin level** according to **Doumas et al., (1981)**
- **Serum globulin calculation** as described by **Doumas and Biggs, (1972)**

- **Determination of serum Transaminases (ALT) and (AST) activities** according to **Reitman and Frankel, (1957).**
- **Determination of serum Alkaline phosphatase (ALP) activity according to Rosalki, (1993).**

(B) Kidney function tests:

- **Determination of serum Creatinine:** according to **(Henry, 1974)**
- **Determination of Urea:** according to **(Patton and Crouch, 1977)**

Statistical analysis: as described by **Snedecor and Cochoran, (1981)**

RESULTS

1- Prevalence of different causes of calve scour

One hundred and fifty diarrheic calves at different farms at Dakahlia and Damietta Governorates were diagnosed by rapid diagnostic kits to identify the causative agent of diarrhea as mentioned in **Table (1) and Figure (1).**

Table (1): Prevalence of different causes of calve scour at Dakahlia and Damietta Governorates

No. of calves	Causative microorganisms			
	Cryptosporidium	Rota virus	Corona virus	E. coli
150	87 (58%)	28 (18.6%)	25 (16.6%)	10 (6.6%)

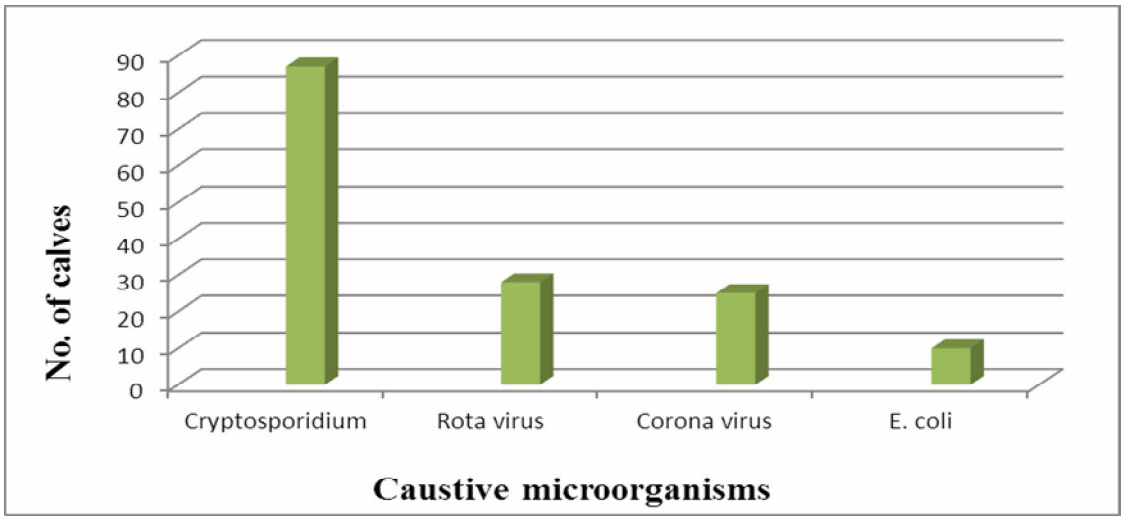

Figure (1): Prevalence of different causes of scour in calves of experiment at Dakahlia and Damietta Governorates.

3- The effect of intramuscular injection of cefquinome (2mg/kg body weight) for 3 successive days on total protein, albumin, globulin, ALT, AST, ALP, urea and creatinine in calves as shown in Table (3).

4- The effect of intramuscular injection of cefquinome (2mg/kg body weight) for 3 successive days on body weight in calves as shown in Table (4).

2- The effect of intramuscular injection of cefquinome (2mg/kg body weight) for 3 successive days on erythrocytic count, hemoglobin content, PCV, MCV, MCH, MCHC, total lukocytic count, neutrophil, lymphocyte, monocyte, basophil, eosinophil and platelets in calves as shown in Table (2).

Table (2): The effect of intramuscular injection of cefquinome (2mg/kg body weight) for 3 successive days on total erythrocytic count, Hb content, PCV, MCV, MCH, MCHC, and total and differential leukocytic count in calves.

(Mean ± S.E) n= 10

Item	Group	zero	1st	2nd	3rd
RBCs(×10^6/ML)	Control	6.94 ± 0.37	8.20 ± 0.20	7.30 ± 0.33	7.20 ± 0.32
	Treatment	6.60 ± 0.44	6.23 ± 0.67*	6.06 ± 0.61*	6.37 ± 0.46*
Hb (gm / dl)	Control	10.38 ± 0.44	8.43 ± 0.96	8.30 ± 0.21	8.60 ± 0.30
	Treatment	7.53 ± 0.86*	6.85 ± 0.75*	6.68 ± 0.66*	6.93 ± 0.57*
PCV (%)	Control	29.30 ± 0.21	29.30 ± 0.26	30.10 ± 0.86	29.50 ± 0.58
	Treatment	25.35 ± 2.63*	22.38 ± 2.77*	21.36 ± 2.52*	21.96 ± 1.89*
MCV (F1)	Control	42.80 ± 0.74	44.40 ± 0.60	45.40 ± 0.88	44.10 ± 0.65
	Treatment	31.76 ± 6.42	35.73 ± 0.85	35.15 ± 0.79	35.91 ± 1.71
MCH (Pg)	Control	11.90 ± 0.31	13.30 ± 0.59	12.80 ± 0.29	14.30 ± 0.33
	Treatment	10.95 ± 0.85*	10.95 ± 0.17*	11.00 ± 0.13*	10.91 ± 0.25*
MCHC (%)	Control	32.70 ± 0.51	34.20 ± 0.67	34.30 ± 0.42	34.90 ± 0.27
	Treatment	29.50 ± 0.45*	30.81 ± 0.57*	31.50 ± 0.54*	31.53 ± 0.41*
WBCs (x 10^3 / ml)	Control	5.90 ± 0.34	4.70 ± 0.42	6.10 ± 0.50	6.10 ± 0.50
	Treatment	9.46 ± 1.39*	9.76 ± 1.73*	9.41 ± 1.23*	9.78 ± 0.91*
Neutrophil (%)	Control	63.10 ± 0.48	60.30 ± 3.17	63.50 ± 0.58	63.40 ± 0.63
	Treatment	57.83 ± 3.09	59.83 ± 3.76	62.16 ± 4.0	53.66 ± 3.56
Lymphocyte (%)	Control	28.50 ± 1.75	29.90 ± 1.10	27.40 ± 1.42	28.60 ± 1.16
	Treatment	30.00 ± 2.92	29.00 ± 3.44	25.66 ± 3.44	33.33 ± 3.06
Monocyte (%)	Control	9.70 ± 0.30	9.90 ± 0.50	9.10 ± 0.45	9.20 ± 0.44
	Treatment	10.50 ± 0.67	10.16 ± 0.60	11.16 ± 0.74*	12.00 ± 0.51*
Basophil (%)	Control	1.10 ± 0.10	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
	Treatment	1.16 ± 0.16	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Eosinophil (%)	Control	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	Treatment	0.16 ± 0.16	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Platelets (nx10^3/ml)	Control	713.40 ± 38.98	781.80 ± 17.06	656.40 ± 24.20	729.10 ± 19.87
	Treatment	771.33 ± 56.93	579.00 ± 31.64*	609.50 ± 72.79	653.33 ± 40.04

* Significant at ($p< 0.05$).

Table (3): The effect of intramuscular injection of cefquinome (2mg/kg body weight) for 3 successive days on total protein, albumin, globulin, ALT, AST, ALP, urea and creatinine in calves.

(Mean ± S.E) n= 10

Item	Group	zero	1st	2nd	3rd
TP (g/dl)	Control	2.35 ± 0.31	1.80 ± 0.20	3.95 ± 0.32	4.20 ± 0.20
	Treatment	2.54 ± 0.18	2.17 ± 0.15	4.30 ± 0.13	2.94 ± 0.27*
ALB (g/dl)	Control	1.89 ± 0.16	1.89 ± 0.14	2.30 ± 0.15	2.90 ± 0.23
	Treatment	1.45 ± 0.11	1.36 ± 0.14	2.48 ± 0.07	1.90 ± 0.20*
Globulin (g/dl)	Control	0.46	-0.09	1.65	1.3
	Treatment	1.09	0.81*	1.82	1.04
ALT (U/L)	Control	6.30 ± 0.59	9.50 ± 0.37	7.40 ± 0.79	8.10 ± 0.23
	Treatment	7.77 ± 1.05	12.66 ± 1.06	9.88 ± 1.12	11.55 ± 2.19
AST (U/L)	Control	8.00 ± 0.25	10.00 ± 0.42	10.00 ± 0.76	9.00 ± 0.44
	Treatment	14.33 ± 1.67*	14.55 ± 1.72*	13.22 ± 1.98*	43.77 ± 18.98*
ALP (U/L)	Control	157.30 ± 8.96	164.80 ± 7.54	97.50 ± 6.49	144.50 ± 9.09
	Treatment	223.33 ± 34.44*	149.55 ± 14.59*	143.55 ± 15.67*	273.44 ± 41.45*
Urea (mg/dl)	Control	17.9 ± 1.05	22.00 ± 1.23	13.40 ± 0.33	11.20 ± 0.35
	Treatment	22.66 ± 3.79*	24.66 ± 2.01	27.22 ± 3.10*	17.55 ± 1.30*
Creatinine (mg/dl)	Control	0.37 ± 0.04	0.46 ± 0.03	0.37 ± 0.03	0.19 ± 0.04
	Treatment	0.90 ± 0.04*	0.70 ± 0.03*	0.57 ± 0.03*	0.72 ± 0.06*

* Significant at ($p < 0.05$).

Table (4): The effect of intramuscular injection of cefquinome (2mg/kg body weight) for 3 successive days on body weight in calves.

(Mean ± S.E) n= 10

Items	Time (Week)	Control	Treatment
Body weight (kg)	zero	31.50 ± 0.81	32.22 ± 0.99
	1st	33.40 ± 0.73	34.11 ± 1.00
	2nd	36.50 ± 0.68	37.44 ± 1.19
	3rd	37.44 ± 1.19	41.22 1.28

DISCUSSION

The major profits in cow calf business are the number of calves and their weight at weaning time; these profits achived by reducing the threating microorganisms at the young age and increasing it's daily body gain. Calf diarrhea still a major cause of productivity and economic loss in cattle and also the cause of high morbidity and mortality in the cattle industry world wide, result from complex interaction of the environment, infectious agents and the calf itself. ***(Bartels et al., 2010 and Randhawa et al., 2012)***

Our study conducted on 150 diarrheic calf at Dakahlia and Damietta Governorate (3-20 days old) to diagnose the main prevalent causative microorganism for calf scour. The more prevalent microorganisms due to cryptosporidium, rota virus, corona virus and E. coli as 87 diarrheic calves due to cryptosporidium (58%), 28 diarrheic calves due to rota virus (18.6%), 25 diarrheic calves due to corona virus (16.6%) and 10 diarrheic calves because of E.coli (6.6%), **Table (1).**

From our result cryptosporidium is the highly prevalent microorganism than rota, corona viruses and E.coli it may be due to all cows vaccinated at dry period by rota, corona virus and E.coli vaccine moreover oral vaccination of calf before colostrum intake using E.coli vaccine plus IgG paste for these microorganisms orally. There is no local or imported vaccine for cryptosporidium, (**Chalmers et al. 2011)**. The prevalence of E.coli was 6.6 %, these diagnosed calves from farm records and there was a non-dry cow vaccination for E.coli nor rota and corona virus.

The present study showed a significant decrease in total erythrocytic count (TEC), hemoglobin content (Hb) and packed cell volume (PCV) in cefquinome treated groups at zero, first, second and third weeks post treatment compared to the control group **(Table 2).**

The obtained data were in agreement with that of **Amer (2017)** who recorded that cefquinome caused a significant decrease in hemoglobin level (Hb) and RBCs count in rats. Moreover, **Mukesh and Suresh (2015)** stated that there was a significant decrease in total erythrocytic count (TEC) at 6^{th} day post treatment with cefquinome. Significant decrease in hemoglobin (Hb) concentration at 3^{rd} day post treatment and significant decrease in PCV at the first day of treatment with cefquinome in buffalo calves. **Anan (2017)** stated that there was a significant decrease in TEC and Hb level in metritic cows treated with ceftiofur.

These data disagree with that obtained by **Shams (2017)** who found a significant increase in hemoglobin (Hb) content in coliform mastitic cows treated with cefquinome (1mg/kg). A significant increase in packed cell volume (PCV) on cefquinome treated cows at the first and second weeks post treatment waw obtained Similarly, **Kishanrao (2016)** found that there was a significant increase in total erythrocytic count (TEC), hemoglobin (Hb) concentration and paked cell volume (PCV) after15^{th} day of treatment with cefquinome in buffalo calwes.

The obtained results showed a significant decrease in mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) in cefquinome treated

groups at zero, first, second and third weeks post treatment comparedto the control group, **(Table 2).**

These data disagree with that obtained by **Maden et al. (2001)** who detected that the intramuscular administration of cefquinome (1mg/kg) in dogs caused a significant increase in mean corpuscular hemoglobin concentration (MCHC) after day 7 post treatment. Similarly **Mukesh and Suresh (2015)** stated that there was a significant increase in values of MCV, MCH and MCHC post treatment with cefquinome in buffalo calves.

The present data mirrored a significant increase in total leukocytic count after cefquinome treatment at zero, first, second and third weeks post treatment compared to the control group, **(Table 2).** This result agree with that of **Shams (2017)** who showed a significant increase in total leukocytic count of coliform mastitic cows at the second week post treatment with cefquinome. Also, **Kishanrao (2016)** detected a significant increase in total leukocytic count (TLC) in day 15 of treatment with cefqquinome in buffalo calves.

Our results disagree with that obtained by **Shpigel (2001)** who showed a significant decrease in total leukocytic count, serum calcium and phosphate with cefquinome treatment. Also, **Shpigel et al. (1997)** stated that there was a significant decrease in total leukocytic count during cefquinome treatment of cows with mastits.

The obtained results showed a non significant decrease in neutrophil % in cefquinome treated groups at zero, first, second and third weeks post treatment compared to the control group, **(Table 2).** This agree with those of **Murphy et al. (1985)** who found that some cephalosporins induced neutropenia. Similarly, **Naftel et al. (1985)** suggested that cephalosporins induced neutropenia due to toxic depression of granulopoiesis and not to the antibody mediated destruction of neutrophils. Furthermore, **Mukesh and suresh (2015)** found that neutrophils were significantly decreased but the values of lymphocytes were increased significantly post treatment with cefquinome in buffalo calves.

Our results evaluated a significant increase in monocyte % in cefquinome treated groups at second and third week post treatment compared to the control group, **(Table 2).** Moreover a significant increase in eosinophil % was recorded in cefquinome treated groups at zero week of treatment compared to the control group. While a significant decrease in thrombocyte % was recorded in cefquinome treated groups at first week post treatment compared to the control group. This confirmed by **Maden et al. (2001)** who reported that 4^{th} generation cephalosporins caused immunologically mediated thrombocytopenia.

This study reflected a significant increase in aspartate transaminase (AST), alkaline phosphatase (ALP), urea and creatinine in cefquinome treated groups at zero, first, second and third weeks post treatment compared to the control group, **(Table 3).**

The present data were supported by the results of **Shams, (2017)** who showed a significant increase in serum alanine aminotransferase (ALT), serum aspartate aminotransaminase (AST) and serum alkaline phosphatase (ALP) activities after cefquinome treatment in coliform mastitic cows. **Amer (2017)** detected a significant increase in ALT, AST, urea and creatinie after cefquinome treatment in rats.Moreover, **Mukesh and suresh (2015)** found that there was a

significant increase in the levels of blood urea nitrogen and creatinine after administration of cefquinome in buffalo calves. This finding is in accordance with **Fanning et al. (1976)** who found that cefoperazone and cephalpthin evoked a nephrotoxic effects which were documented as a rise in the blood urea. Similarly, **Mitchell (1977)** reported that some cephalosporins as cephaloridine have a nephrotoxic effect. **Lurban (1989)** detected that cefexime induced abnormal liver function manifested as elevation of ALT and AST activities. Moreover**, Fekety (1990)** mentioned that cefquinome caused a temporary increase in serum ALT activity. **Zimmerman (1999)** stated that other cephalosporins as cefprozil, cefminox and ceftriaxone induced an increase in serum ALT activity. It has been reported that cephalosporins had some hepatotoxic effect**.**

Our results were disagree with those recorded by **Kishanrao (2016)** Who showed that there is no difference changes in ALT, AST, ALP, urea and creatinine plasma levels after cefquinome administration in buffalo calves. Similarly, **Mukesh and suresh (2015)** concluded that repeated administration of cefquinome did not influence the plasma activities of ALT, AST, GGTP and ALKP in buffalo calves. Moreover, **Maden et al. (2001)** observed that ALT, AST, ALP, Ca, Na and K levels did not change after administration of cefquinome in dogs.

Our results showed a significant decrease in total protein and albumin in cefquinome treated groups at third week post treatment compared to the control group, on the other hand, there was a significant increase in globulin at zero and first week post treatment with cefquinome compared to the control group, **Table (3).**

The obtained results were supported by the result of **Maden et al. (2001)** who observed that there was decrease in total protein level in dogs treated with cefquinome. Also, **Shpigel et al. (1997)** showed that there was a decrease in total serum protein, serum calcium, phosphate and sodium during cefquinome treatment of cows with mastits.

Our study showed a non-significant increase in calves body weight in cefquinome treated groups at zero, first, second and third weeks post treatment compared to the control group, **Table (4).**

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الملخص العربي
تأثير السيفوكينوم في علاج الإسهال في العجول

محمد جبر السيد*، محمد مصباح الديسطي**، دعاء محمد محمد وحيد

قسم الأدوية – كلية الطب البيطري جامعة المنصورة*، معهد بحوث صحة الحيوان المنصورة**

أجريت هذه الدراسة لمعرفه مدي فاعليه السيفوكينوم لمعالجة الإسهال في العجول. إستخدم عدد ٢٠ من العجول المصابة بالإسهال أعمارهم بين ٣-١٥ يوم وتم تقسيمها إلي مجموعتين (١٠عجول / المجموعة). المجموعة الأولي تم معالجتها بالسيفوكينوم بجرعة ٢ ملغم / كجم عضل لمدة ثلاث أيام متتالية والمجموعة الثانية هي المجموعة الضابطة لم يتم حقنها في العضل. وبينت النتائج إرتفاع معنوي في عدد كرات الدم البيضاء والجلوبيولين وإنزيم الأسبرتات ترانس أمينيز وإنزيم الفوسفاتيز القاعدي واليوريا والكرياتينين. لكن كان هناك نقص معنوي في عدد كرات الدم الحمراء وتركيز الهيموجلوبين وحجم خلية كرات الدم الحمراء ومتوسط نسبة الهيموجلوبين فى الدم وعدد الصفائح الدموية والخلايا الليمفاوية والبروتين الكلى والألبيومين وذلك عند المعالجة بالسيفوكينوم مقارنة بالمجموعة الضابطة.