Effect of Antiviral drug (Ribavirin) on Very Virulent Infectiou Bursal Disease Viral Infection in Chickens

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Abstract

Studies were carried out to evaluate the pathogenecity and coagulat disorders in 42-day-old chickens infected with vvIBDV or vaccinated v intermediate vaccine or intermediate plus vaccines associated with or with ribavirin treatment .Pathogenicity studies revealed that vvIBDV (S-95) produc acute disease with sever clinical picture and high mortalities reached to 60% white egg-type chickens. Pathogenicity study indicated increased survival rat chickens treated with ribavirin after challenged with vvIBDV, as 34 chicks surv from 35 chicks. It may be related to ribavirin-enhanced immune system (T-cel Study of coagulation disorders indicated significant defects in extrinsic a intrinsic clotting systems, as the virus lead to increase of bleeding time, clott time, and prothrombin time which probably account for the rapid death and se hemorrhagic lesions.

Introduction

Infectious bursal disease (IBD) is an acute highly contagious viral infection young chickens firstly described by Cosgrove (1962).The disease leading direct and indirect significant economic losses to the worldwide poultry indus (Chettle et al., 1989 ; Van Den Berg et al., 1991).The direct economic losses IBD is due to morbidity and mortality rate while the indirect impact is due immunosspression of infected birds (Van den Berg,2000). IBD is a hig contagious immunosuppressive disease caused by infectious bursal disea virus (IBDV), which is classified as amember of the family Birnaviridae (Van d Berg, 2000 and Rautenschlein, 2003).The virus has predilection to replicat the lymphoid cells of the bursa of fabricius causing severe inflammatory chan resulting in bursal atrophy. Although the bursa of fabricius is considered a target organ for IBDV (Muller et al., 1979 and Hirai et al., 1981) , changes oc in other organs including spleen , thymus , kidney and liver (Henry,198 Sharma et al. (1993 & 2000). Elankumaran et al. (2002) mentioned that cecal tonsils , and the bone marrow might serve as non bursal lymphoid tissu supporting IBDV replication.

The very virulent form (vvIBDV) caused by highly pathogenic strains o appeared at late eighties in Europe and is currently expanding quite rap world-wide. This primarily causes high levels of mortalities up to 60% wi couple of days, generally occurring between 3 and 5 weeks of a (Lukert,1996). Furthermore in1986 very virulent (vv) strains of IBD ha emerged in Europe ,which can cause up to70% flock mortality in lay pullets and 100% in specific pathogen-free (SPF) chicken (Chettle et 1989 and Van Den Berg ,1991). In Egypt (in the summer of 1989), sev outbreaks of very virulent IBD (vvIBDV), similar to those reported European countries in both vaccinated and non-vaccinated floc associated with high mortalities up to 70% in replacement layer pullets a

30% in meat-type birds (El-Batrawi, 1990; Ahmed, 1991 and 1993; Khafagy et al., 1991). The present study was directed towards Determination coagulation disorders associated experimental vvIBDV infection or vaccination with live IBDV vaccines associated with or without ribavirin treatment.

Material and methods

1-Chicks:

Sufficient, number of one-day-old commercial egg-type (L.s.L) which possessed maternal antibodies against IBD, acquired from their parents.

2-Blood samples:

Blood samples were obtained by cardiac puncture. Blood samples were placed into tubes containing sodium citrate for measuring coagulation parameters.

3-IBD viruses

a-Two types of commercial live IBDV vaccines one "intermediate" (D78) strain and one "intermediate plus" "hot" vaccine (2512) obtained from the local agencies, were used in the study.

b- A local field isolate of vvIBDV isolated and identified by Sultan (1995) in the form of bursal extract was diluted 1: 10 in phosphate buffer saline (PBS), which killed 72% of 7-week-old susceptible commercial male chickens and designated as (S-95), was used during experimental infection.

4-Antiviral drugs :

Ribavirin was kindly supplied by Pharma Swede-Egypt Pharmaceutical Companey.

5-For citrated blood:

One part of sodium citrate (3.8%) was added to nine parts of blood.

6-For prothrombin time:

Mammalian prothrombin time kit (BIO Merieux, Mareyl Etoile, France) obtained from local agencies.

- Citrated plasma.

7-Indirect Enzyme Linked Immunosorbent Assay (ELISA):

Commercial ELISA kits ProFlock supplied by Synbiotics Corporation, 11011 via Frontera, San Diego. CA 92127

Experimental design of laboratory experiment:

Group (no)	IBDV	Treatment	Assesment for 7 days PI
1	vvIBDV	Ribavirin	1-Clinical signs and mortality. 2- Gross lesions. 3-follow up MDA by ELISA test. 4- B:B ratio and B:B index. 5- Seroconversion by ELISA test. 6- Antigen detection of bursal hemogenate of dead birds. 7 -Coagulation disorders: BT, CT, and PT.
2	vvIBDV	non	
3	IBDV intermediate vaccine(D78)	Ribavirin	
4	IBDV intermediate vaccine(D78)	non	
5	IBDV intermediate plus vaccine (2512)	Ribavirin	
6	IBDV intermediate plus vaccine (2512)	non	
7	non	Ribavirin	
8	non	non	

(1) Field dose/bird via oculo-nasal route.

(2) The chickens were subjected to oculo-nasal challenge with 100 ul / bird.
(3) PI = post inoculation.
(4) B: B ratio = Bursal body weight ratio (Sharma et al ., 1989).
(5) B: B index = Bursal body weight index (Lucio and Hitchner, 1979).
(6) Serological tests were used (ELISA).
(7) Bt = Bleeding time (Bigland,1964)
(8) CT = clotting time (Benjamin, 1978).
(9) PT = prothrombin time (Coles, 1986).

RESULTS

I. Result of Pathogenicity study:

Results of waning of MDA in commercial white egg-type male chickens:
ELISA = Enzyme-linked immunosorbent assay

Age/ days	Birds (n)	ELISA titers	
		Range	Means ± sd
7	5	15929 – 18811	17759.4± 525.1
14	5	13953 – 16574	
21	5	6307 – 16056	15031.6 ± 452.5
28	5	2307 – 5984	13556.2 ± 1842.9
35	5	1358 – 3565	4554.2 ± 647.9
42	5	763 - 4310	1982.8 ± 406.2
			1806.8 ± 638.9

Sd = standerd deviation
N =Number

Table(2): Results of mortality rate at day post inoculation of chickens challenged with vvIBDV or vaccinated with intermediate or intermediate plus vaccines associated with or without ribavirin treatment at 42-day-old age:

Group No.	Birds No.	Pattern of mortality DPI							mortality		Percipitinogen detection in BF	
		1	2	3	4	5	6	7	Total (N)	%	Dead	survivors
1	35	٠	٠	1	٠	٠	٠	0	١	2.68	1/1	0/34
2	٢٥	٠	٠	10	11	٠	٠	0	٢١	٦٠	21/21	0/14
3	٢٥	٠	٠	٠	٠	٠	٠	0	٠	٠	-	-
4	٢٥	٠	٠	٠	٠	٠	٠	0	٠	٠	-	-
5	٢٥	٠	٠	٠	٠	٠	٠	0	٠	٠	-	-
6	٢٥	٠	٠	٠	٠	٠	٠	٠	٠	٠	-	-
7	٢٥	٠	٠	٠	٠	٠	٠	٠	٠	٠	-	-
8	٢٥	٠	٠	٠	٠	٠	٠	٠	٠	٠	-	-

(1) = simultaneous vvIBDV (Sultan, 1995) and Ribavirin (2)= vvIBDV Sultan (1995)
(3) = simultaneous Intermediate vaccine (D78) and Ribavirin (4) = intermedia
vaccine (D78) (5) =simultaneous intermediate plus (2512) vaccine a
Ribavirin 6=intermediate plus (2512) vaccine (7)= ribavirin treatme
(8) = non treated. DPI= day post inoculation

Table (3): Results of Bursal : Body weight ratio at day post inoculation of chickens challenged with vvIBDV or vaccinated with intermediate or intermediate plus vaccines associated with or without ribavirin treatment at 42-day-old age.

Group	DPI 1	2	3	4	5	6	7
1	4.59 ± 0.38 A	4.24 ± 0.60 AB	3.37 ± 0.52 B	2.44 ± 0.25 C	2.91 ± 0.34 B	2.48 ± 0.35 BC	2.05 ± 0.60 BC
2	4.68 ± 0.15 A	4.06 ± 0.14 B	5.86 ± 0.25 A	3.51 ± 0.22 BC	2.90 ± 0.34 B	1.88 ± 0.02 C	1.54 ± 0.08 C
3	4.97 ± 0.40 A	4.38 ± 0.61 AB	4.86 ± 1.11 AB	6.27 ± 0.90 A	4.86 ± 0.48 A	3.36 ± 0.64 ABC	3.85 ± 0.28 A
4	4.46 ± 0.39 A	4.70 ± 0.45 AB	4.34 ± 0.35 AB	4.89 ± 0.28 AB	4.45 ± 0.66 AB	3.40 ± 1.03 ABC	3.36 ± 0.33 AB
5	5.47 ± 0.53 A	4.63 ± 0.09 AB	4.42 ± 0.32 AB	3.93 ± 0.34 BC	3.62 ± 0.50 AB	2.40 ± 0.36 BC	2.39 ± 0.47 ABC
6	4.61 ± 0.96 A	4.18 ± 0.27 AB	4.74 ± 1.16 AB	4.39 ± 0.71 B	4.49 ± 0.41 AB	2.31 ± 0.34 BC	3.00 ± 0.68 ABC
7	4.61 ± 0.47 A	5.75 ± 0.16 A	4.17 ± 0.57 B	4.30 ± 0.51 B	4.39 ± 0.41 AB	3.59 ± 0.23 AB	3.77 ± 0.35 A
8	5.65 ± 0.41 A	3.85 ± 0.68 B	4.14 ± 0.39 B	4.12 ± 0.32 B	4.37 ± 0.60 AB	4.33 ± 0.44 A	3.78 ± 0.49 A

Groups:

(1) = simultaneous vvIBDV (Sultan, 1995) and Ribavirin
(2)= vvIBDV Sultan (1995)
(3) = simultaneous Intermediate vaccine (D78) and Ribavirin
(4) = intermediate vaccine (D78)
(5) =simultaneous intermediate plus (2512) vaccine and Ribavirin
(6) = intermediate plus (2512) vaccine
(7)= ribavirin treatment
(8) = non treated.
DPI= day post inoculation
number of observation per mean = 3.
values are means ± standard errors.
means in the same column (treatments within day) followed by the same capital letter are not significantly different at (P = 0.05).

Table (4): Results of Bursal : Body weight index at day post inoculation chickens challenged with vvIBDV or vaccinated with intermediate or intermedia plus vaccines associated with or without ribavirin treatment at 42-day-old age.

Group	DPI 1	2	3	4	5	6	7
1	0.81 ± 0.07 A	1.10 ± 0.15 B	0.81 ± 0.13 B	0.59 ± 0.06 C	0.67 ± 0.08 B	0.57 ± 0.08 B	0.54 ± 0.16 BC
2	0.82 ± 0.03 A	1.06 ± 0.04 B	1.41 ± 0.06 A	0.85 ± 0.05 BC	0.66 ± 0.08 B	0.43 ± 0.01 B	0.41 ± 0.02 C
3	0.88 ± 0.07 A	1.14 ± 0.16 AB	1.17 ± 0.27 AB	1.53 ± 0.22 A	1.11 ± 0.11 AB	0.78 ± 0.15 AB	1.02 ± 0.08 A
4	0.79 ± 0.07 A	1.22 ± 0.12 AB	1.05 ± 0.09 AB	1.19 ± 0.07 AB	1.02 ± 0.15 AB	0.78 ± 0.24 AB	0.89 ± 0.09 AB
5	0.97 ± 0.09 A	1.20 ± 0.02 AB	1.07 ± 0.08 AB	0.95 ± 0.08 BC	0.83 ± 0.12 AB	0.55 ± 0.08 B	0.63 ± 0.13 ABC
6	0.81 ± 0.17 A	1.08 ± 0.07 B	1.14 ± 0.28 AB	1.07 ± 0.17 B	1.03 ± 0.09 AB	0.53 ± 0.08 B	0.79 ± 0.18 ABC
7	0.82 ± 0.08 A	1.49 ± 0.04 A	1.01 ± 0.14 B	1.04 ± 0.12 B	1.00 ± 0.09 AB	0.83 ± 0.05 AB	1.00 ± 0.09 A
8	1.00 ± 0.07 A	1.00 ± 0.18 B	1.00 ± 0.09 B	1.00 ± 0.08 B	1.00 ± 0.14 AB	1.00 ± 0.10 A	1.00 ± 0.13 A

Groups:
(1) = simultaneous vvIBDV (Sultan, 1995) and Ribavirin
(2)= vvIBDV Sultan (1995)
(3) = simultaneous Intermediate vaccine (D78) and Ribavirin
(4) = intermediate vaccine (D78)
(5) =simultaneous intermediate plus (2512) vaccine and Ribavirin
(6) = intermediate plus (2512) vaccine
(7) =ribavirin treatment
(8) = non treated.
DPI =days post inoculation
number of observation per mean = 3.
values are means ± standard errors.
means in the same column (treatments within day) followed by the same capi letter are not significantly different at (P = 0.05).

II- Results of coagulation disorders:

Table (5): Results of bleeding time (BT) in seconds at day post inoculation o chickens challenged with vvIBDV or vaccinated with intermediate or intermediat plus vaccines associated with or without ribavirin treatment at 42-day-old age.

Group	DPI 1	2	3	4	5	6	7
1	216.00 ± 10.79 A c	241.67 ± 30.31 AB bc	291.67 ± 6.69 B b	543.33 ± 11.67 B a	281.67 ± 33.78 B b	192.33 ± 9.40 BC cd	156.00 ± 19.76 AB d
2	161.33 ± 20.74 AB e	275.33 ± 34.28 A d	469.33 ± 39.10 A b	920.67 ± 30.34 A a	380.67 ± 17.29 A c	280.67 ± 4.06 A d	190.00 ± 0.58 A e
3	175.00 ± 28.16 AB ab	172.33 ± 3.93 CD ab	144.67 ± 22.10 DE ab	191.67 ± 17.85 D a	122.67 ± 13.28 D b	114.67 ± 2.85 D b	132.33 ± 0.67 AB ab
4	115.33 ± 5.90 B bc	198.00 ± 22.11 BC a	115.00 ± 12.77 E bc	109.00 ± 9.00 E c	135.00 ± 17.79 D bc	171.67 ± 3.53 BCD ab	146.33 ± 2.91 AB abc
5	157.00 ± 11.00 B ab	161.00 ± 24.54 CDE ab	210.67 ± 74.31 C a	199.33 ± 8.11 D ab	146.00 ± 23.58 D b	180.67 ± 7.67 BC ab	147.33 ± 4.84 AB b
6	115.33 ± 7.86 B c	131.33 ± 22.06 DE c	156.67 ± 24.55 CDE bc	258.00 ± 22.50 C a	209.33 ± 7.42 C ab	229.33 ± 9.60 AB a	161.67 ± 1.33 AB bc
7	143.00 ± 17.79 B a	145.00 ± 18.93 CDE a	159.33 ± 7.06 CDE a	115.67 ± 9.94 E a	173.67 ± 6.96 CD a	165.33 ± 3.28 CD a	126.67 ± 2.40 B a
8	124.00 ± 11.79 B ab	106.00 ± 3.46 E b	176.00 ± 9.29 CD a	176.00 ± 8.19 D a	136.33 ± 13.97 D ab	136.00 ± 13.01 CD ab	113.33 ± 1.67 B b

Groups:
(1) = simultaneous vvIBDV (Sultan, 1995) and Ribavirin
(2)= vvIBDV Sultan (1995)
(3) = simultaneous Intermediate vaccine (D78) and Ribavirin
(4) = intermediate vaccine (D78)
(5) =simultaneous intermediate plus (2512) vaccine and Ribavirin
(6) = intermediate plus (2512) vaccine
(7) = ribavirin treatment
(8) = non treated.
DPI =days post inoculation
number of observation per mean = 3.
values are means ± standard errors.
means in the same column (treatments within day) followed by the same capita letter are not significantly different at (P = 0.05)

Table (6) :Results of clotting time (CT) in seconds at day post inoculation of chickens challenged with vvIBDV or vaccinated with intermediate or intermedia plus vaccines associated with or without ribavirin treatment at 42-day-old age.

Group	DPI						
	1	2	3	4	5	6	7
1	39.00 ± 7.37 A b	64.33 ± 7.22 A b	153.00 ± 49.57 A a	65.00 ± 15.70 A b	74.33 ± 4.33 AB b	56.67 ± 4.67 A b	55.33 3.53 A b
2	73.33 ± 10.14 A a ab	49.67 ± 5.17 A b	89.00 ± 4.93 B a	68.33 ± 7.51 A ab	92.33 ± 3.71 A a	84.33 ± 1.20 A ab	68.33 2.19 A ab
3	47.67 ± 6.49 A a	57.33 ± 9.53 A a	42.33 ± 6.33 C a	37.67 ± 2.60 A a	53.67 ± 1.76 B a	59.67 ± 4.33 A a	62.33 2.33 A a
4	46.33 ± 3.67 A a	72.67 ± 12.71 A a	57.00 ± 10.15 BC a	65.00 ± 10.00 A a	78.67 ± 12.12 AB a	62.67 ± 2.40 A a	66.00 1.15 A a
5	39.33 ± 8.33 A cd	36.00 ± 0.58 A cd	126.00 ± 49.44 A a	31.67 ± 4.41 A d	51.00 ± 6.66 B bcd	70.67 ± 4.48 A bc	79.67 1.45 A b
6	41.00 ± 3.46 A b	50.67 ± 2.60 A b	85.67 ± 18.41 B a	38.33 ± 8.01 A b	75.33 ± 5.17 AB ab	78.00 ± 4.58 A ab	68.33 3.71 A ab
7	42.33 ± 9.56 A b	45.67 ± 3.38 A b	84.67 ± 26.27 B a	33.33 ± 0.67 A b	47.33 ± 14.38 B ab	51.00 ± 4.04 A ab	48.33 1.67 A ab
8	37.67 ± 3.93 A a	33.00 ± 1.53 A a	69.33 ± 22.81 BC a	45.00 ± 6.43 A a	43.00 ± 5.13 B a	48.00 ± 1.73 A a	49.00 4.58 A a

Groups:
(1) = simultaneous vvIBDV (Sultan, 1995) and Ribavirin
(2)= vvIBDV Sultan (1995)
(3) = simultaneous Intermediate vaccine (D78) and Ribavirin
(4) = intermediate vaccine (D78)
(5) =simultaneous intermediate plus (2512) vaccine and Ribavirin
(6) = intermediate plus (2512) vaccine
(7) = ribavirin treatment
(8) = non treated.
DPI =days post inoculation
number of observation per mean = 3.
values are means ± standard errors.
means in the same column (treatments within day) followed by the same capi letter are not significantly different at (P = 0.05).

Table (7): Results of prothrombine time (PT) in seconds at day post inoculati of chickens challenged with vvIBDV or vaccinated with intermediate intermediate plus vaccines associated with or without ribavirin treatment at 4 day-old age.

Group	DPI						
	1	2	3	4	5	6	7
1	101.33 ± 18.84 BC c	239.33 ± 77.70 B b	480.00 ± 63.51 A a	181.67 ± 11.70 AB bc	142.67 ± 22.98 B bc	145.67 ± 2.96 A bc	146.3 ± 4.84 A bc
2	259.33 ± 50.47 A c	754.67 ± 109.92 A a	425.00 ± 138.41 A b	227.00 ± 17.95 A c	245.00 ± 14.05 A c	176.33 ± 1.67 A c	177.0 ± 2.65 A c
3	136.00 ± 20.23 BC a	105.67 ± 32.69 CD a	112.67 ± 9.77 B a	112.67 ± 4.06 B a	106.00 ± 6.00 B a	115.33 ± 0.88 A a	114.3 ± 2.03 A a
4	186.33 ± 35.03 AB a	152.33 ± 55.11 BC a	172.00 ± 13.32 B a	99.00 ± 6.03 B a	140.00 ± 8.50 B a	134.33 ± 0.67 A a	132.3 ± 1.20 A a
5	177.67 ± 23.92 AB a	101.00 ± 51.50 CD a	151.67 ± 3.33 B a	106.00 ± 2.31 B a	152.67 ± 5.21 AB a	148.33 ± 2.60 A a	148.6 ± 3.33 A a
6	133.67 ± 17.32 BC a	106.67 ± 7.06 CD a	165.00 ± 3.00 B a	123.33 ± 8.65 B a	192.00 ± 4.04 AB a	171.00 ± 2.00 A a	175.6 ± 2.33 A a
7	42.67 ± 8.69 C a	54.67 ± 4.48 CD a	107.67 ± 7.45 B a	101.00 ± 6.24 B a	111.33 ± 2.40 B a	112.00 ± 1.00 A a	113.3 ± 0.88 A a
8	38.33 ± 12.68 C a	41.33 ± 5.78 D a	101.33 ± 3.67 B a	102.67 ± 3.38 B a	101.67 ± 1.67 B a	101.67 ± 1.20 A a	102.0 ± 1.53 A a

Groups:
(1) = simultaneous vvIBDV (Sultan, 1995) and Ribavirin
(2)= vvIBDV Sultan (1995)
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(6) = intermediate plus (2512) vaccine
(7) =ribavirin treatment
(8) = non treated.
DPI =days post inoculation
number of observation per mean = 3.
values are means ± standard errors.
means in the same column (treatments within day) followed by the same capita letter are not significantly different at (P = 0.05).

Discussion

At first, it was important to investigate the pathogenicity of the fi isolate (Sultan, 95) and intermediate vaccine or intermediate plus vaccir associated with or without ribavirin treatment for susceptible commercial e type chickens under controlled laboratory condition. Table.1 revealed t maternally derived antibodies are gradually dropped from 1st week till the week. These results supported by Khafagy et al. (1991) who followed up I maternally derived antibodies in chickens. The ELISA titers (mean) was 1775 ± 525.1 at 1 week,15031.6 ± 452.5 at 2 weeks, 13556.2 ± 1842.9 at 3wee 4554.2 ± 647.9 at 4 weeks, 1982.8± 406.2 at 5 weeks, and 1806.8± 638.9 a weeks.

Maternal derived antibodies (MDA) played an important role in protection chickens at early age 3-5 weeks of age that ensured by Al-Natour et al. (20 who demonstrated the important role of maternally derived antibodies and th titers in protecting the newly hatched chicks against IBDV when exposed to vi at different ages.In the present study, the daily observation revealed typ signs of IBD which appeared on the IBDV-infected birds including ruf feathers, depression, anorexia, trembling, watery-whitish diarrhea, vent pick and prostration. The mortality and many of the clinical signs of IBD might caused by depletion in the circulating hemolytic complement resulting from formation of immune complexes (Ivani and Morris,1976 and Ley et al., 1979 by depletion in some clotting factors leading to hemorrhage (Skeels et al., (19 a, 1979-b).

Moreover, the observed clinical signs, morbidity and mortality rates matched with those previously reported by Inoue et al. (1994), and Lima et al. (2005). Differences in mortality rates could be attributed to the variable levels of resi maternal antibodies at time of infection. In all cases, all mortalities occurred DPI, and dead birds showed sever hemorrhagic lesions typical of IBDV infect IBDV antigen could be demonstrated in all bursal homogenate from birds succumbed within 2-4 days to infection, but not in those from survivors 10 This finding is of significance from the diagnostic point of view in that detec of IBDV antigen in the bursa by the AGPT should be done on acutely affe birds. It was apparent from these results that the 42-day-old chickens w most susceptible and suitable to use for evaluation of other parameters.

Postmortem lesions characteristic for IBDV were observed .The observed g lesions were similar to those previously reported by Inoue et al.(1994), Rodriguez-Chavez et al. (2002).

As shown in tables 3 & 4 the vvIBDV-inoculation in group (1), caused signifi decrease of bursal weight to body weight ratio and bursal body weight in While in group group (2), there was significant increase of bursal body we ratio at 3rd DPI followed by significant decrease at 6th and 7th DPI significant increase of bursa body weight index at 3rd DPI followed by signifi decrease at 6th and 7th DPI. The bursal atrophy might be resulted from replication of the virus in the bursa of fabricius (Sharma et al., 2000) On

other hand ribavirin treated group showed significant increase of bursal to body weight ratio and bursal to body weight index at 2nd day post treatment.

Secondary, coagulopatheis associated with IBDV infection or intermediate vaccine or intermediate plus vaccine associated with or without ribaviri treatment in 42-day-old susceptible chickens are presented in tables 6, 7, and It was found that all values obtained from the parameters used to reflect the effect of extrinsic and intrinsic clotting system (bleeding time, clotting time, and prothrombine time, respectively) during 7DPI.

Tables 5,6 and 7 showed that the vvIBDV caused a significant increase o bleeding time, clotting time, and prothrombine time. These results are supporte by those observed by Koster et al. (1972) who found prolonged thromboplasti time in 23-day-old chickens infected with IBDV and decreased clotting factors II V, VII (prothrombine factors) which attributed to disseminated intravascula coagulation. Moreover, Kumar and Rao (1991); Giambrone et al. (1978-b), an Chang and Hamilton (1982) reported prolonged clotting time and prothrombin time in combined infection of aflatoxicosis and IBD. Moreover, Bigland an Triantophyllopoulos (1961) speculated the prolonged prothrombin time due t the lack of coagulation factors.

Cho et al. (1974) and Skeels et al. (1979-b), explained the prolonged clottin times to depletion of circulating level of hemolytic C (complement) from th formation of immune complexes at sites of viral replication or a depletion i some clotting factors which result in hemorrhage or both. In addition. Moreove Mayahi et al., (2003) showed prolonged mean prothrombin time (which is measure of extrinsic clotting system), the mean whole blood recalcification tim (which related to factors I , V ,VIII, IX and X) and the mean activated partia thromboplastin time (which related to factors VIII, IX, X and XI) in broiler chick inoculated with IBDV by intrabursal route at day and 14-day-old. But the IBD had no effect up on the clotting time (which related to V and X factors an prothrombin synthesis in liver) up to 7 days while the clotting time prolonged a 14 days of age. Also the authors revealed that the effect of IBDV on clotting tim related to age of birds as with increasing the age the effect was mor severe.Other groups (3, 4, 5 & 6) showed various significant changes tha depend on severity and pathogenesis of viral strain. On the other hand the grou treated with ribavirin showed no significant changes of coagulation parameters.

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الملخص العربى

تأثير العقاقير المضادة للفيروسات (ريبافيرين) على عدوى فيروس التهاب كيس فابريسى الشديد الضرواة فى الدجاج

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أجريت الدراسات المعملية لمعرفة التغيرات الإكلينيكية والباثولوجية والسيرولوجية عند حقن فيروس مرض الجمبورو شديد الضراوة في الدجاج البياض التجاري القابل للإصابة. كما تم دراسة التغيرات في ظاهرة تجلط الدم حدث نفوق في المجموعة المصابة بالعترة شديدة الضراوة للفيروس بنسبة ٦٠% بينما كانت نسبة النفوق في المجموعة المصابة بالعترة شديدة الضراوة والمعالجة بالريبافرين ٢,٦٨% بينما لم يكن هناك أي وفيات في المجموعات الأخرى.

١- أوضح فحص الطيور وجود أنزفة دموية وآفات تشريحية مميزة لعدوى فيروس كيس فابريسى .

حدث زيادة معنوية في زمن النزيف (BT) في المجموعات المصابة بالعترة شديدة الضراوة للفيروس سواء عولجت اولم تعالج بالريبافرين ،المجموعة المحصنة باللقاح الحي متوسط الضراوة مع العلاج بالريبافرين و المجموعة المحصنة باللقاح الحي شديد الضراوة سواء عولجت أو لم تعالج بالريبافرين .

وجد زيادة معنوية في زمن التجلط (CT) من اليوم الثاني إلى اليوم السابع حيث سجلت أعلى زيادة معنوية في اليومين الثالث والخامس في المجموعات المصابة بالعترة شديدة الضراوة سواء عولجت أو لم تعالج بالريبافرين. أيضا كان هناك زيادة معنوية عند اليوم الثالث في المجموعة المحصنة باللقاح الحي متوسط الضراوة مع العلاج بالريبافرين .

حدثت زيادة معنوية في البروثرومبين تايم (PT) عند اليوم الثالث في المجموعات المصابة بالعترة شديدة الضراوة للفيروس سواء عولجت اولم تعالج بالريبافرين بينما كان هناك زيادة معنوية عند اليوم الثاني فالمجموعة المحصنة باللقاح الحي متوسط الضراوة فقط.