Study of Ivermectin effect on the bovine warts

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Abstract

Cutuneous warts in bovine are benign tumors induced by virus belongs to papillomaviruses family . Ivermectin drug used in treatment of endo and ectoparasites in animals and to treat the bovine warts at a dose 300 microgroms / Kg . B . wt . sub cutaneously .

Ten cattles were be used in this expirement , five of them injected subcutaneously at the base of the wart and other Five injected also subcutaneously upper of the scapular bone faraway the wart position .

Statistical analysis for obtained results reveals presence of singnificantly raised ($P<0.05$)in the mean of total white blood cells count from (5.480±1.064)cell before treatment and reach to (7.380±0.511)cell after treatment and the mean of lymphocytes rate from (35.200±6.685)% before treatment and reach to (65.400±11.929) %after treatment .Also reveals significant depression ($P<0.05$) in the mean of neutrophils and monocytes rates from (57.800±6.685)% , (4.200±0.836)% before treatment and reach to (31.200±11.322)% , (1.600 ± 1.140)% after treatment respectively .

Eight cattles were being recover from sum of ten cattles and the clearance rate reach's to 80% without any side effect on the animals so the mean of total white blood cells counts for recovered animals are showing in table -1 are being normal was (5.940±0.698) also the mean of differential percentage of the white blood cells is returned normal , neutrophils was (60.400±0.270)% , lymphocytes (33.600+3.209)% , monocytes (4.400±0.894)% , eosinophils (1.200±0. 447)% ,and basophils (0.600±0.548)% .

Introduction

Cutaneous warts in bovine are benign tumors induced by host – specific papillomaviruses which are entered through any skin abrations .

Papillomaviruses are being in six types ; bovine papilloma virus (BPV)-1 , BPV-2 and BPV-5 , which cause fibropapillomas ;and BPV-3, BPV-4 and BPV-6 , which cause true epithelial papillomas. Warts sometimes occur around ear tags , face , neck , back , udder and has been observed in squamous cell carcinoma of bovine eyes in solid outgrowths of epidermis ,may by sessile or pedunculated and has cauliflower – like , and occur predominantly in young animals . The lack of susceptibility of adults to natural infection being ascribed to immunity acquired by apparent or inapparent infection when young (Radostitsts,etal.,2000).

Diagnosis is based on clinical signs and confirmed by histopathology and this is represented by section -1 which reveals the histopathology of untreated bovine skin wart . Also the diagnosis can be done by DNA identification by polymerase chain Reaction (PCR) technique in biopsy or tissues scraping . The treatment is done by surgical removal or cryosurgery (Gibbs,etal.,2004) vaccination with autogenous vaccines (Jhonson,etal.,2001).

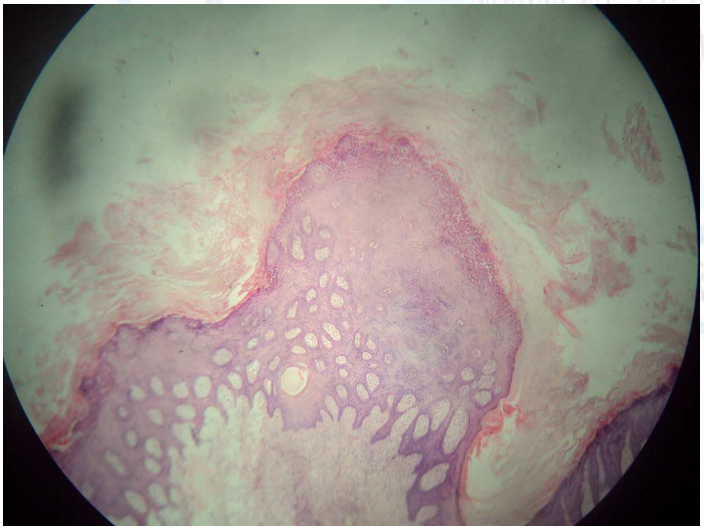
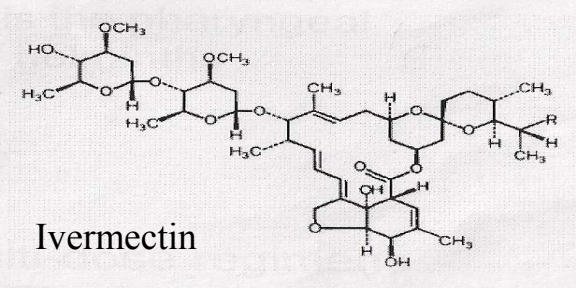


Figure -1 : Represent the histology of untreated wart . This histological picture is done in laboratory of pathology in Baghdad veterinary collage.

The objective which be selected in this study is have chemical formation shows below .



(Yates and Wolstenholme , 2004).

Ivermectin is macrocyclic lactones are products or chemical derivatives of soil microorganisms belonging to the *Streptomyces avermitilis* fungus, and the main uses of ivermectin in treatment of intestinal helminthes infections as strongyloidiasis , onchocerciasis and heart worm ,also it is active agents in treatment of ectoparasites like ticks and lice (Yates and Wolstenholme,2004)

Materials and Methods

1- Ivermectin 1%

Ivermectin is manufactured by saudi pharmaceutical company

2- Animal groups

Infected animals were divided according to the site of injection of drug into two groups :

Group - A

In this group five animals (at different age and sex) were treated at a dose 300 micrograms /Kg. B . Wt .(Bogan and Mckellar.,2000) ,subcutaneously interior base of the wart from different aspects same dose in locations is repeated after eleven days according to the information which had been takes from the manufacture corporation.

Group – B

In this group five animals (at different age and sex) were treated at a dose of 300 micrograms /Kg . B . Wt , subcutaneously in the region of upper of the scapular bone faraway the wart .same dose in other site of the intend region is repeated every eleven days continuously at least four doses till the wart is degraded .

3-Five milliliters of blood was be collected randomly before and after the treatment from five animals only after 33 days and they are reserves in K3 EDTA vials to determinate the whole and differential white blood cells count . From five recovered animal , five milliliters of blood has been takes to determinate the whole and differential white blood cells count .

4- Histopathology to the untreated and defunct wart tissue after treatment in each infected animal is done in laboratory of pathology and histology of Baghdad and Diyala veterinary college .

Statistical Analysis

Statistical analysis is done at calculation of t .value dependency in all treatments and the comparison between its values and values of tabloid - t. (Zar,1984) .

Results and Discussion

This study is supported by pictures (1a,b,c) after injection of drug in the base of the wart ,and pictures (2a,b,c) after injection of drug subcutaneously .

These pictures shows the gradual loss in size of wart after each injection and sloughing to the dead tissue which occurs after treatment.

a b c

Figure -1 : represent the wart in the medial aspect of the tail. : a-before the treatment .b-after the treatment.c. the degraded wart.

a b c

Picture-2 :a- represent the wart before the treatment . b-after the treatment.c- the degraded wart.

These results may be become from three reasons ; the first is due to cytotoxic effect of Ivermectin on carcinic cell of the wart as the same inhibiting effect of calvatic acid which is extracted from *Calvatia craniformis* fungus on the carcinoma (Hamao ,etal.,1975),also the ivermectin extracted from soil fungus and may be possess this ability , so our imagination are coming from gradual loss in size after every subcutaneous injection of drug , also the wart mass is losing vitality and can be seeable from the owners .

Kim et al .(1992) observed that protein – bound polysaccharides extracted from cultured *C . craniformis* mycelium suppressed the growth of sarcoma in mice by up to 74 .1 % . The anti – tumor activity of at ieast one of extract fraction referrd to as calvatane was believed to be as a result of immuno potentiation rather than cytotoxicity .

The second reason is may be due to the Ivermectin effect on the cellular immune response of the animal and this effect is elicits from the results in table -1 which shows significant elevation ($P<0.05$) in the rate of lymphocyte cells after treatment by Ivermectin , so the mean of values is raised in all animals from (35.200±6.418) before treatment and reachs to

(65.400±11.929) and this elevation accompanied by significant elevation (P<0.005) in total white blood cells counts ,so the mean values is raised in all animals from (5.480 ±1.064) thousand cells before treatment and reachs to (7.380 ±0.511) thousad cells after treatment .Also there is no statistical srgnification (P>0.05) in values of eosinophils and basophils before and after treatment.

The two eleviations in total count of white blood cells and in percentage in lymphocyte cells were be share in raising the immunity of the infected animals and cause degradation of the wart tissue .These results are supported by other study which is suggest an immunopotentiating effect of Ivermectin at higher doses (Sajid,etal.,2007) .

One of the components of the lymphocytes is T – cell , it can be distinguished from others by peresence of special receptor on its surface called T cell receptor (TCR) and play a central role in cell – mediated immunity as virally infected cells and tumor cells (Schwarz and bhandoola ,2006) . There is other T – cell called natural killer T – cells (NKT-Cell) , is able to recognize and eliminate some tumor cells (Barton,etcol.,2000) .

Also there is significant depression (p<0.05) in neutrophils rate and monocytes rate, so the mean values is depressed from the normal values (57.800±6.6854)% before treatment and reaches to (31.200 ±11.322) and from (4.200±0.836) %before treatment and reaches to (1.600 ±1.140)% after treatment respectively and these results don't have any side effects on the animal health along the period of treatment .

We dose found in scientific researches any thing may be refers to Ivermectin effect on papillomas ,but our idea about local injection of Ivermectin to treat the wart was been elicited from the irritation which occurs in site of injection and it is coming in agreement with other study on Ivermectin subcutaneous injection which is caused significant dermal thicknss at the site of injection in all treated Animals (GoKulut,etal.,2008). Also the idea is supported by other study which reveal the presence of the blood plasma in the site of injection due to the damage of the blood vesseles include vein and artery (Preston and Derricott, 1998) .

This damage of nutrient blood vessels in the base of the wart lead to death or the necrosis of the carcinic cells and sloughing from its origin on the skin and this image followed by this applied study which is considered as the third reason .

Table -1: Represent number of cattle and white blood cells count

The Material	Cattle Number	WBC /mm3 and rates of different cells (Mean ± standard deviation)													
		Before treatment						After treatment							
		Total WBC Count	N	L	M	E	B	Total WBC Count	N	L	M	E	B		
Ivermectin	5	5.8	55	39	4	1	1	8.0	45	52	1	2	0		
		6.8	52	41	5	1	1	7.8	20	79	0	0	1		
		6.0	68	25	3	3	1	7.3	19	77	2	2	0		
		4.6	61	33	4	2	0	7.0	35	59	3	2	1		
		4.8	53	38	5	3	1	6.8	37	60	2	1	0		
		5.480 ± 1.064	57.800 ± 6.685	35.200 ± 6.418	4.200 ± 0.836	2.000 ± 1.000	0.800 ± 0.447	7.380* ± 0.5119	31.200* ± 11.322	65.400* ± 11.929	1.600* ± 1.1402	1.400 ± 0.894	0.400 ± 0.547		
		Mean and Standard Deviation													

After recover					
Total count	**N**	**L**	**M**	**E**	**B**
4.8	60	34	5	1	0
6.6	57	36	4	2	1
6.3	64	29	5	1	1
5.8	59	37	3	1	0
6.2	62	32	5	1	0
5.940 ± 0.698	60.400 ± 0.270	33.600 ± 3.209	4.400 ± 0.894	1.200 ± 0. 447	0.600 ± 0.548

In general the Ivermectin possess the ability to determinate and stop the growth of bovine wart followed by degradation especially in early stage of formation better than in advance stage without any side effect was be reflected on the general health of recovered animals; also the total white blood cell counts are returned to normal value was (5.940 ±0.678) with normal differential percentage of the cells .

This ability is raising the rate of clearance to (80%) in aperiod moderated from 2 – 3 months because one of the cases didn't responded to treatment because it has a large size with broad base and the drug may be didn't reach to nutrient blood vessels lead to failure of experiment and picture – 3 show the case .

Picture – 3 : unsuccessful treatment to this wart by Ivermectin .

The ivermectin have partial failure in treatment of the second case .The site of the wart was be beside the perianal region but the treatment was done not in the base of the wart but faraway the site and repeated every 11 days for 3 injection lead to destroy the right side of the wart then the nowner decide to do surgical operation to remove the left side and the picture (4a,b) represent this case .

Picture – 4a:a:represent the wart on the two side of the perianal region before the treatment.

4b : represent the removal of the right portion of the wart after by ivermectin treatment

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