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DIMETHYL SULFOXIDE (DMSO)* IN THE TREATMENT OF ACUTE EXPERIMENTAL LAMINITIS IN HORSES (With 2 Table and 6 Figures)

Ву

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داي مثيل سلفواكسيد في علاج الإلتهاب الحاد المخلق للصفائح الحساسة المغلفة لعظمة الحافر في الخيول

أديب حنا ، لطفية فهمي ، علي حجازي ، محمد بركات

تم في هذا البحث الاحداث التجريبي لإلتهاب حاد في الصفائح الحساسة المغلفــة لعظمة الحافر في الخيول وذلك بتغليتها علائق مركزة من الكربوهيدرات وعلاج هــــدا الإلتهاب بإستخدام الداي مثيل سلغوأكبيد في خلال م ساعات من بداية أعراضه حيــت سجل التحسن في الأعراض الإكلينيكية بعد العلاج · وجد أن الداي مثيل سلغوأكسيـــد (٧٠ / _ ٢٠) له تأثير أكثر من الفينيل بيوتازون كمضاد للإلتهاب وموسع للأرعيـــة الدمرية · أوضحت النتائج أنه بعد تحسن بعض الأعراض الإكلينيكية حدث دوران لعظمة الحافر وتغيرات باثولوجية في أنسجة الحافر ·كما أوضحت النتائج أن إستخدام العلاج المذكور أها إلى إعادة الدورة الدموية إلى حالتها مع تقليل الهدم بالصفائح الحساسة ·

SUMMARY

Acute experimental laminitis was induced in horses by feeding carbohydrate ration, therapy of acute laminitis started within 8 hours from the beginning of the signs. The different criteria of clinical improvement were recorded. It was found that DMSO (70-90%) was effective and potent as anti-inflammatory and vasodilator than phenylbutazone therapy. In addition, the results showed that after clinical improvement, the animals showed degrees of pedal rotation and histopathological changes within the hoof tissues. Laminitis therapy had potent effects on restortion of the disturbed circulation within the hoof, and at the same time it minimized epidermal destruction.

^{*:} DMSO (Diamond laboratories, INC.).

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INTRODUCTION

Dimethyl sulfoxide (DMSO) was known to be an extraordinary chemical derivrative of lignin (KLIGMAN, 1965). DMSO had the ability to penetrate unbroken skin, potentiate other compounds and possessed significant anti-inflammatory properties (KLIGMAN, 1965 and JACOB, 1982). It was found to have a potent pain reliever, a mild local vasodilator, antibacterial and diuretic effects and capable of making soluble collagen (ROBERT KNOWELS, 1982).

Clinical application of DMSO on horses, cattle, dogs and cats proved that the drug was safe and effective in treating many inflammatory conditions of musculo-skeletal disorders and lameness (KOLLER, 1976).

Much had been written about the mechanism and pathogenesis of experimental laminitis in the horse (OBOL, 1984; GARNER, 1980 and BARAKAT, 1986).

The purpose of this communication was to evaluate the clinical efficacy of DMSO in the treatment of acute experimental laminitis in comparison to current therapy (phenylbutazone). Furthermore, radiographic and histopathological studies were conducted for assessments of clinical improvement.

MATERIAL and METHODS

Experimental laminitis was induced in 10 clinically normal horses, by feeding a high carbohydrate ration (BARAKAT, 1986).

Within eight hours after the appearance of the symptoms of acute laminitis (O"bel grade 3 lameness) these horses were classified into two groups. Group (I) five horses recieved therapy consisting of mineral oil (paraffin oil) for coating the gastro-intestinal tract. On the first day of treatment ACTH* (50 IU) was injected intra-muscularly, followed by another dose of ACTH (25IU) after 12 hours, associated with I/V. fluid therapy (4 liters of normal saline 0.9% Nacl, and liters of commercially prepared sterial pyrogen free electrolyte solutions) for 4-5 days until the animal general condition improved. Intravenous injections of sodium bicarbonate 1.5% for three successive days to overcome acidosis. 60 ml (DMSO 70% solution with 500 ml glucose 5% were administered daily intravenously during the course of treatment, in addition 10 gm methionine** were also given intravenously. DMSO (90%) solution mixed with Xylocaine*** 2% were applied topically above the coronet and digit. Systemic antibiotic (Streptopencid****) was administered for 3-5 days.

^{*:} ACTH (Laboratoire choory, Paris).

^{**:} Methionine (BDH chemicals Ltd poole England).

^{***:} Xylocaine (Soder-Ialje, Swedin).

^{****:} Streptopencid (CID, Egypt).

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Group (II) five horses were treated with the previous regimen except the use of phenylbutazone I/V injections at a dose rate of 4.4 mg/Kg. bwt. twice on the first days, followed by a dose 4.4 mg/Kg. bwt. daily for four days. Then 2.2 mg/Kg. bwt. daily untill response to therapy occurred.

The different criteria for monitoring the efficacy of treatment were encountered in Tables (1 and 2).

Emperical observation and evaluation of two regimens were recorded on days 3,5,7,9 and 12 as compared to pre-treatment. Radiographic evalutions were undertaken on group (I) on the 10 day of treatment and group (II) on the 13th day.

Histopathological samples were taken under the influence of general narcosis and nerve block. Frontal mid-line sections 2 cm x 2 cm from the dorsal wall of the hoof at the toe were taken to include the whole layers of the hoof (stratum externum, stratum medium and stratum lamellatum). Section was carried out under freezing microtome at -30 C into thin sectioned (5Um) and stained with H & E stain.

RESULTS

Clinical signs of experimental laminitis O'bel grade 3 lameness appeared 32±0.48 hours after giving the animals a laminitis inducing ration. Diarrhea developed in all horses, increased body temperature, depression adipsia, dehydration, hurried respiration, flaring up the nostriles, oedema of the cornet and fetlock, stiffness of both fore limbs. The horses moved most reluctantly and vigorously resisted attempts to lift a fore foot.

The treatment of horses were strated within 8 hours after the appearance of lameness. Tables (1 & 2) showed clinical evaluation of the two regimens in two groups. It was noticed that, injections of sodium bicarbonate 1.5% and electrolytes therapy intravenously in the two groups gives improvement in respiration and general conditions.

Observations in group (I) treated with DMSO (90%) marked clinical improvement in different parameters were strated from 4th and 5th days. The horses were found to be clinically normal within 7-9 days table (1). Group (II) horses treated with phenylbutazone, the clinical improvement was less and started on the 7th and 9th days, and marked improvement was usually evident after 10 to 12 days of treatment.

Radiographic studies revealed a slight palmar rotation in PIII. (Fig. 1), inspite of the normal gait of the animals.

The histopathological evaluations in two groups revealed laminar epithelial hyperplasia and keratinizations. The dermal and epidermal laminae were fused together forming epithelial sheets (Fig. 2), the dermal laminae appeared hypertrophied with elongation of the secondary epidermal laminae. The laminar structures were separated

Table (1): Evaluation of laminitis treatment with Dimethylsulfoxide (DMSO).

arameters.	Pre-Treatment	After treatment evaluation.				
ar director 3.		Day 3	Day 5	Day 7	Day 9	
Temperature (c°)	39.7	38.2	37.8	37.8	37.5	
Pulse / minute	80/m	60/m	50/m	50/m	50/m.	
Digital Pulsa-	80/m	55/m	48/m	42/m	42/m	
tion/ minute					ent on de lan estern du cita	
Condition of the	severe	slight	slight	disappeared	disappeared.	
coronet and	hotness	hotness	hotness			
Hoof wall						
Oedema of the	severe	severe	slight	disappeared	disappeared	
coronet.	est sentroll coll rectal could be com-			semine and en	Mag and far fall to share a constant	
Oedema of the	severe	slight	slight	disappeared	disappeared	
fetleck joint.			Jones College	ules som se	a respective	
Stiffness of	severe	severe	Moderate	slight	disappeared	
ooth fore-limbs.	stiffness	stiffness	stiffness		1555 June 1979	
loof tester test	severe	severe	Moderate	slight	disappeared	
hise avorqui	pain	pain	pain	, eus ig in	No an Alberta	
urning in a	severe	severe	Moderate	slight	disappeared	
mall circle.	pain	pain	pain	svenski teolog	- Touppeur Cu	
ameness at	severe	severe	Moderate	slight	disappeared	
alk	eli alla ni mana		riplic a drain	avat vojbujeva	a. Juppeul Ed	

The degree of judgment.

- Slight signs of laminitis

severe signs of laminitis

- disappeared (the animal clinically normal)

Moderate signs. laminitis

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Table (2): Evaluation of laminitis treatment with phenylbutazone.

Parameters	Pre-treatment:	After treatment evaluati						
	Evaluation	Day 3	Day 5	Day 7	Day 9	Day 12		
emperatures (c°)	39.8	38	37.4	37	37	37		
ulse/minute	70/m.	- 70/m.	63/m.	50/m	48/m	48/m		
igital pulsati-	70/m.	55/m	50/m	50/m	44/m	44/m		
n/minute								
ondition of	severe	severe	Moderate	Moderate	Slight	disappeased		
oronet and hoof	hotness	hotness	hotness	hotness	hotness			
all.								
edema of the corone	t. severe	severe	Moderate	slight	disap	disappeared		
edema of the	severe	severe	Moderate	Moderate	slight	disappeared		
etlock joint.					14,911 757			
Stiffness of	severe	severe	severe	Moderot	slight	disappeared		
ooth fore-limbs	stiffness	stiffness	stiffness	stiffness	stitness.			
loof tester test	severe	severe	Moderate	slight	slight	disappeared		
urning in a small	pain	pain	pain	pain	pain			
ircle.								
ameness at	severe	severe	severe	Moderate	slight	completely		
valk.					impro 'vement	improved		

The degree of judgment.

Severe signs of laminitis Slight signs of laminitis.

Moderate signs of laminitis. Disappeared. The animal clinically normal.

from the tubular layer by a new intermediate degenerative layer containing these called "pseudotubular structures" in different stages of degeneration and hyalinization. The tubular layer the tubules appeared elongated (Fig. 3,4 & 5).

The histopathological changes in hind limbs of both groups displayed several laminar structural changes. The laminar structures appeared atrophied and in some cases devoid of its primary epidermal laminae (Fig. 6).

DISCUSSION

Acute experimental laminitis (O'bel grade 3 lameness) appeared after 32+0.48 hours post feeding of laminitis inducing rtion. The therapy was started in the horses as early as possible i.e. within 8 hours, owing to early morophological changes (O,BEL, 1948), and laminar epithelial hyperplasia and hyperkeratinization were noticed secondary to vascular and mechanical damage (BARAKAT, 1986).

Carbohydrate overload for inducing laminitis showed some degree of septicemia and shock with systemic circulatory changes (HOOD, 1979; HOOD & STEPHEN, 1985 and CLARK, GARNER & HATFIELD, 1982). Circulatory changes within the foot were noticed as first serious events. The use of DMSO in the treatment of acute laminitis had clinical efficacy as anti-inflammatory, pain reliever and vasodilator properties. In this respect, BRAYTON (1986) reported that DMSO has a direct anti-inflammatory effect on tissues through its ability to scavenger free radicals that are known to increase with tissue damage, associated with inflammation, ischemia and bacterial infection.

DE LA TORRE (1985) reported that DMSO possesses anti-thrombogenic effects. He postulated that the drug has direct effects on the prostaglandine- thromboxane and platelate systems, and this interfere with the bicohemical, vascular and morphological processes that leads to ischemic tissue injures.

According to the clinical results, DMSO injections in these horses showed clinical improvement, the heat in the feet is depressed, pain is less and the bounding digital pulse resolves, this improvement starting from the third and fourth day of treatment.

The intravenous administration of DMSO has been documented in acute traumatic injury to the head with resultant increased intracranial pressure and cerebral oedema (CAMP et al., 1981 and DE LA TORRE, 1985). Therefore, the intravenous administration of DMSO (70%) demonstrated to be effective anti-inflammatory agent in treating acute laminitis. Moreover, the local application of DMSO (90%) associated with local anaesthesia allowed the animals to stand and walk normally. This improvement could be attributed to the vasodilator effect of DMSO in the foot circulation which had been depreciated within the hoof during laminitis onset (COFFMAN, 1970; HOOD, 1979 and BARAKAT, 1986).

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The systemic injections of fluid therapy with ACTH during the first day of treatment, have an indirect influence upon osomotic pressure of the local tissues, and the blood was brought quickly enough to prevent any damage to the laminae (LAWSON, 1954).

The radiographic examinations in two groups after clinical improvement revealed a minimal degree of palmar rotation of PIII. inspite of normal gait of the animals. Furthermore, histopathological evaluations in two groups displayed changes in the dermal and epidermal architecture and the hallmark of chronicity in the hoof tissues appeared, with the formation of inter-mediate degenerative layer. Previously, the presence of this layer have been documented in chronic experimental laminitis (BARAKAT, 1986), as a sequelae to degenerative processes in the laminar tissues, due to depreciation of its blood supply, accompanied by ischemic necrosis of the laminae.

One can suggest that, the therapy of acute laminitis restored the vascular disturbances within the hoof tissues, at the same time, it decreased or minimized the epidermal destructions. Furthermore, the two regimens had clinical efficacy in tretment of acute experimental laminitis. However, the effect of DMSO therpy was shown to be better than phenylbutazone.

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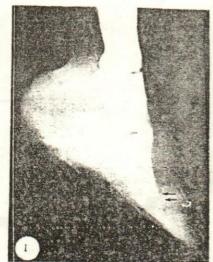
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LEGENDS

- Fig. 1: Lateral radiograph in a horse for-limb (foot) after treatment revealed, a minimal palmar rotation of PIII.
- Fig. 2: C.S. of the laminar layer at the toe (for limb) after treatment, Note: The dermal and epidermal laminae forming epithelial sheets. H & E stain. X 10.
- Fig. 3: The laminar layer at the toe (C.S.): The intermediate degenerative layer" containing" pseudotublar structures H & E stain. X- 10.
- Fig. 4: Intermediate degenerative layer in different stages of degeneration and keratinization. H & E stain. X-10.
- Fig. 5: The stratum medium at the toe (C.S.): The tubular layer, the tubules appeared elongated. H & E stain. X 10.
- Fig. 6: C.S. of the laminar layer at the toe (hind limb): Degeneration of the laminar structures with absence of the primary epidermal laminae in some laminar structures. H & E stain. X 10.

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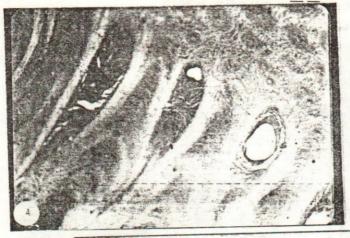


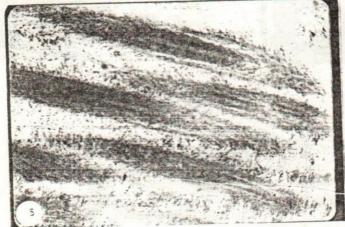




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