Myonecrosis And Skin Sloughing Management After Defaults Of Drug Injections

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ABSTRACT

The study was carried on 35 animals of different species (25 equine, 8 cattle and 2 dogs). These were admitted to the surgery clinic, department of surgery faculty of veterinary medicine, Zagazig University within five years (2002-2007). The animals come with different surgical problems observed following administration of drug injection. The age of the affected animals ranged from 2months - 9 years. The injected drugs were a combination of Penicillin & Streptomycin (Pentomycin, Univet LTD, Ireland) I/M, Oxytetracycline (Vetwic, El Nasr Pharmaceutical Chemical Co. A.R.E.) I/M, Terramycin LA (Pfizer Inc, NY, USA) I/M, Imizol (Schering-Plough Animal Health) S/C, Ultrabac vaccine (Pfizer Inc, NY, USA) S/C, Phenylbutazone (Butaphenyl Univet LTD, Ireland) S/C & I/M, Flunixine Meglumine (Finadyne, Shering-Plough Animal Health) I/M, Cafozal (Alexandria Co. Egypt) I/M, Procaine Adrenaline (Alexandria Co. Egypt) S/C, Levamizole 10% (Memphis Co. Cairo- Egypt) & Ucimizole (Amoun Pharmaceutical Co.) S/C and Ivermectin (Ivomec) S/C. Indications of drugs injection were for feeding improvement and prophylactic against infection and parasites in addition to the use of anti-inflammatory drugs were for rheumatic and traumatic lameness. Injection of procaine adrenaline in a puppy at the base of the tail was for docking. Intramuscular and subcutaneous injections were the recorded routes and the neck and gluteal regions were the common sites of injection. The surgical disorders were noticed at the site of injection and the surrounding tissues following injection by 3-5 days. They were differentiated according to the type of affection and degree of tissue damage into five stages. Cellulitis, abscess, phlegmone, myonecrosis and skin sloughing were the common clinical signs. Aggressive antibiotic therapy, non-steroidal anti-inflammatory, surgical fenestration, debridement, lavaging and local dressing were the used methods of treatment. The wounds were commonly managed by wound contraction and epithelialization. Outcome was good in all cases. Fibrotic myopathy was observed after healing of myonecrosis and different sizes of scar tissue formation was observed after healing of skin wounds. It is recommended to increase the number of drugs used in equine therapy through different pharmaceutical companies. In addition, the use of each drug is through its specific route and in its specific animal species. The pamphlet of drugs must be applied. Intravenous injection is the prime route and the intramuscular injection is preferred in the cervical muscles. Multiple injection at one area is avoided and strictly aseptic precautions in injections (needle, syringe, drugs and site of injection) must be put in consideration.

INTRODUCTION

Necrosis of muscle and skin sloughing usually occurs as results of infected wounds, or from iatrogenic damage following the injection of irritant or caustic drugs *(1-5)*. Edema, erythema and cutaneous necrosis were recorded under many of drug injection. The injection of antibiotics seldom results in local infection, but quite frequently intramuscular injections results in local myonecrosis and infection subsequently develops *(1)*. The injection of other drugs more commonly results in infected sites, and the most serious of these infections are those due to *Clostridia* sp bacteria, in which gas production and extensive myonecrosis produce a life-threatening situation *(1-3,6-11)*. Local damage of this type within a muscle may have very serious immediate toxic consequences, affect the function of the specific mass of muscle, adjacent nerves and blood vessels and other structures. Other than the infection accompanied with injection and the irritation of drugs, skin eruption was reported with many of antibiotics, anti-inflammatory, antiparasitic and vaccines *(1,12-18)*. Drug

eruption is rare, variably pruritic, pleomorphic cutaneous or mucocutaneous reaction to a drug. The incidence of drug eruption in large animals is unknown. The pathologic mechanism of drug eruption is thought to involve types I, II, III and1V hypersensitivity reactions *(16,17,19,20)*. The addition of a vasoconstrictor such as epinephrine was used to increase the intensity, prolong anesthetic activity and reduce the potential of toxicity. The use of local anesthetic drugs containing a vasoconstrictor often causes tissue necrosis along wound edges, especially in thin-skinned animals *(21,22)*.

The present study was aimed to record the cases having disorders in the skin and subcutaneous tissues resulting from different drug injections. These disorders were examined and evaluated. Treatment was attempted according to the degree of tissue damage and the outcome of treatment was recorded. The precautions to avoid occurrence of these conditions are discussed and recommended.

MATERIAL AND METHODS

Case history

This study was carried on 35 animals of different species (25 equine, 8 cattle and 2 dogs). These were admitted to the surgery clinic, department of surgery faculty of veterinary medicine, Zagazig University within five years period (2002-2007). The animals come with various surgical problems observed following administration of drug injection. The affected animals ranged from 2months - 9 years of age. The history of occurrence of these conditions was taken; including; type and dose of drug, route and site of injection, disease for which drug injected, and onset with sequence of stages of the affection observed in addition to if there was trials of treatment. The animals were clinically examined and the observed disorders were evaluated.

The clinical findings and treatment

The admitted animals were classified and treated according to the type of observed affection and degree of tissue damage:

I-Cases in which localized closed swelling at the site of injection and without accompanied systemic illness, were treated by cold application on the swelling three times daily and injection of non-steroidal anti-inflammatory drug phenylbutazone (Butaphenyl, Univet LTD, Ireland) 10ml I.V. for 3-5 days.

II- Cases in which localized closed swelling at the site of injection and accompanied by systemic illness were treated by iodine ointment 5% or Icthyol ointment 10% two times daily on the swelling until softening and ripening. The ripened swellings were opened, evacuated, drained and swabbed by povidone iodine 10%. Systemic antibiotics, Penicllin & streptomycin, (Pen-strept, Norbrook) 4ml/kg I/M was used for five days and phenylbutazone (Butaphenyl) 10ml I/V was used for three days. The cavity of the swelling was daily dressed until it healed by second intention.

III- Cases in which diffuse inflammation of the injected area and extended to the whole limb, were treated by intravenously injected of Gentamycin 10% (Univet LTD, Ireland) 6ml/100kg BW diluted in 500ml isotonic normal saline or by a high dosage of crystalline penicillin (22,000 IU/kg q 4 h) I/V for five days. Phenylbutazone (Butaphenyl) 10ml I/V was injected for 3-5 days. Localized areas of skin necrosis and fistula formation were curetted, drained and dressed.

IV-Cases in which localized skin necrosis and sloughing at the site of injection were treated by removal of all debris and necrotized tissues and flushing of the wounds by povidone iodine 2%. Counter opening and drainage treated the observed fistulous tracts or gaps. Nitrofurazone ointment (Furaderm, Amoun Pharmaceutical Co.) was applied for five days. Tetravet Aerosol, (Bonac Laboratories LTD, NewZeland) antibiotic spray was used on the wound until complete healing supervened.

V- Cases in which massive skin necrosis and sloughing of large areas of soft tissues were treated by trimming of all necrotized and sloughed tissues until reaching the healthy tissues. The fistulous tracts were curetted and drained. Counter opening of the gap areas were performed. The necrotized patches of muscle were removed and the resulted bleeding was controlled. The large wounded areas were flushed by normal saline and swabbed by povidone iodine 10% in addition to a mixture of 700 Vaseline, 300ml glycerin and 10gm neomycin 20%, (Vetwic, El Nasr Pharmaceutical Chemical Co. ARE.) or Baneocin, (Pharco pharmaceuticals Alexandria, Biochemie Austria) was applied.

Surgical interference was accomplished under tranquilization by propionyl promazine (Combelen, Bayer) 0.15mg/kg I/V in equine and Xylazine 2% (Rompun, Bayer) 0.05mg/kg I/V in cattle and 1mg/kg I/M in dogs.

Postoperative management

In cases accompanied by systemic illness, Gentamycin 10% 4ml/100kg BW or a combination of penicillin & streptomycin (Pen-strep) 4ml/kg was used for five days and phenylbutazone (Butaphenyl) 10ml I/V was used for three days. The wounds were daily dressed until healing was completed by second intention.

Antitetanic serum was routinely given in animals having wounds of equine species.

RESULTS

From the case history, the injected drugs were a combination of Penicillin & Streptomycin (Pentomycin, Univet LTD, Ireland) I/M, Oxytetracycline (Vetwic, El Nasr Pharmaceutical Chemical Co. ARE.) I/M, Terramycin LA (Pfizer Inc, NY, USA) I/M, Imizol (Schering-Plough Animal Health) S/C, Ultrabac vaccine (Pfizer Inc, NY, USA) S/C, Phenylbutazone (Butaphenyl Univet LTD, Ireland) S/C & I/M, Flunixine Meglumine (Finadyne, Shering-Plough Animal Health) I/M, Cafozal (Alexandria Co. Egypt) I/M, Procaine Adrenaline (Alexandria Co. Egypt) S/C, Levamizole 10% (Memphis Co. Cairo-Egypt) & Ucimizole (Amoun Pharmaceutical Co.) S/C and Ivermectin (Ivomec) S/C (Tab 1).

Most of the affected animals were apparently healthy before injection. The indications of injected drugs were for feeding improvement and prophylactic against infection and parasites in addition to the use of anti-inflammatory drugs were for rheumatic and traumatic lameness. Injection of Procaine adrenaline in a puppy at the base of the tail was for docking. Intramuscular and subcutaneous injections were the recorded routes and the neck and gluteal regions were the common sites of injection. Different surgical disorders were observed at the site of injection and the surrounding tissues following the injection of drug by 3-5 days. They were differentiated into five stages (Table 2):

1- Localized inflammatory swelling at the site of injection was observed in eight horses injected antimicrobial drugs (Pentomycin, Oxytetracycline and Terramycin LA) in the muscle of the neck and gluteal region. (Fig. 1). The animals were depressed and unwilling to move their necks or hind limbs. Complete cure of animals was noticed within 1-2 weeks of systemic and local treatment.

2- Small-localized areas of skin necrosis and sloughing ranged from 3-5cm were detected in five horses injected Imizol and Ultrabac vaccine subcutaneously in the neck. Dermatoses were observed at the site of injection within two weeks and then necrosis and sloughing of the covering skin supervened by 2-3 days (Fig. 2&3). Complete healing of the observed wounds was attempted in 10 days of treatment.

3- Diffuse swelling with or without ulcerated areas and fistulous tracts was manifested in 10 animals (three horses, mule, donkey, 4 cattle and dog) injected intramuscularly or subcutaneously anti-inflammatory drugs (Butaphenyl & Finadyne) and Cafozal. Diffuse inflammation was noticed at the site of injection and surrounding tissues

(Fig. 4&5&6). Stiffness gait and rise of temperature were observed. The phlegmonous swellings were accompanied by necrotized areas of skin and fistulous tracts draining pus in some cases (Fig. 5&6). Complete cure was observed after 2-3 weeks of treatment through high doses of antibiotics and draining of the fistulae.

4- Moderate skin necrosis and sloughing of the injected area 15-20cm were observed in seven animals (a puppy, 2 horses and 4 cattle). The puppy was injected procaine adrenaline around the base of tail for docking and the other animals were injected subcutaneously levamizole and Ucimizole in the neck (Fig. 7&8&9). The systemic disturbance was detected. Complete healing of wounds after wound dressing were obtained in a month.

5- Massive skin necrosis and sloughing of the injected area and its surrounding more than 40cm diameter were observed in five horses injected Ivermectin subcutaneously in the neck (Fig. 10 &11). Large areas of dry hard slough skin in the neck and pectoral region was noticed. The subcutaneous tissues and muscles had signs of necrosis with fistulous and gap formation. Removal of necrotized tissues and lavaging the wounds by antiseptics initiated the production of healthy granulation tissue for healing (Fig.12). Complete healing of wounds was noticed within two months of treatment.

Outcome of treatment:

The fate of healing of these affections resulted either a firm dense scar tissue near the muscle (fibrotic myopathy) (Fig. 13) or scar tissue formation in the skin. Mild unnoticed scar (Fig. 14), moderate observed scar (Fig. 15) and large deformed scar (Fig.16) were resulted depending on the degree of myonecrosis and skin loss from necrosis and sloughing..

Table 1. The type and dose of the drug injected in animals

Type of drug	Dose of drug	Route of injection	Site of injection	Affected animals	Age of animals (years)
Pentomycin	4ml/100kg	I/M	Gluteal	Horse	3y
Oxytetracycline	1ml/10kg	I/M	Neck &Gluteal	5 horses	2-9y
Terramycin LA	1ml/10kg	I/M	Gluteal	2 horses	3&6y
Imizol	2ml/100kg	S/C	Neck	4 horses	2-7y
Ultrabac vaccine	5ml	S/C	Neck	Horse	3Y
Butaphenyl	2ml/dog 10ml/large animals	S/C&I/M	Neck & gluteal & thigh	Horse, mule, donkey, 4 cattle & dog	2y, 3y, 3y, 8months-3y & 3months
Finadyne	10ml	I/M	Gulteal	Horse	5Y
Cafozal	20ml	I/M	Thigh	Horse	1.5Y
Procaine adrenaline	6ml	S/C	Around tail	Dog	2months
Levamisole 10% & Ucimizole	20ml	S/C	Neck	2 horses & 4 cattle	2-8Y
Ivomec	8-10ml	S/C	Neck	5 horses	1.5-5Y

Table 2.Type and degree of tissue damage in relation to the type of drug injected

Groups	Degree of tissue damage	Type of drugs injected	Number of animals
I	Localized swelling at site of injection (cellulitis & paniculitis)	**Pentomycin, Oxytetracycline & Terramycin LA**	8
II	Small swelling with localized areas of skin sloughing	**Imizol and Ultrabac vaccine**	5
III	Diffuse swelling (phlegmon) with or without ulcerated and fistulous areas	**Butaphenyl, Finadyne & Cafozal**	10
IV	Moderate skin necrosis and sloughing in area	**Ucimizole & procaine adrenaline**	7
V	Massive skin necrosis and sloughing observing myonecrosis	**Ivomec**	5

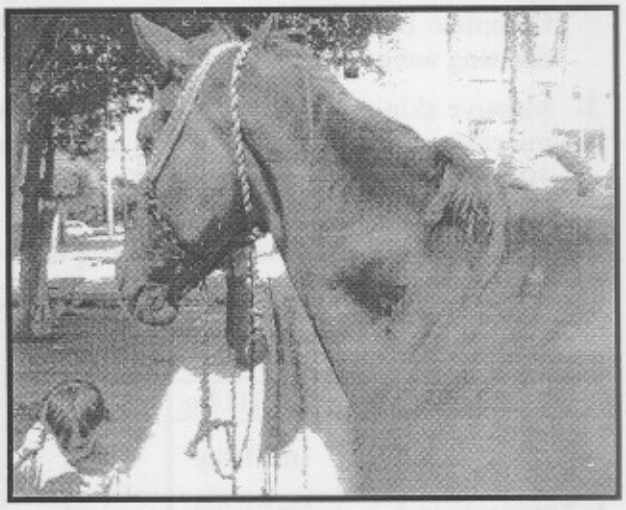

Fig. 1: Swelling at the lateral aspect of the neck of a horse after intramuscular injection of oxytetracycline

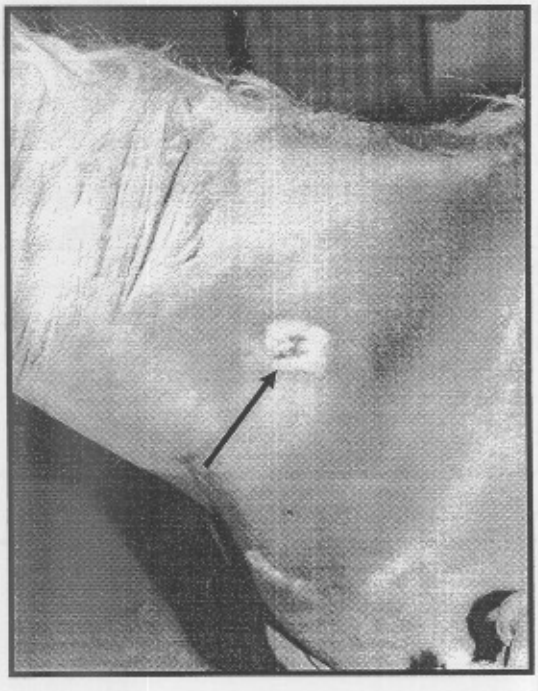

Fig. 2: Swelling and dermatosis at the lateral aspect of the neck of a horse after intramuscular injection of Imizol

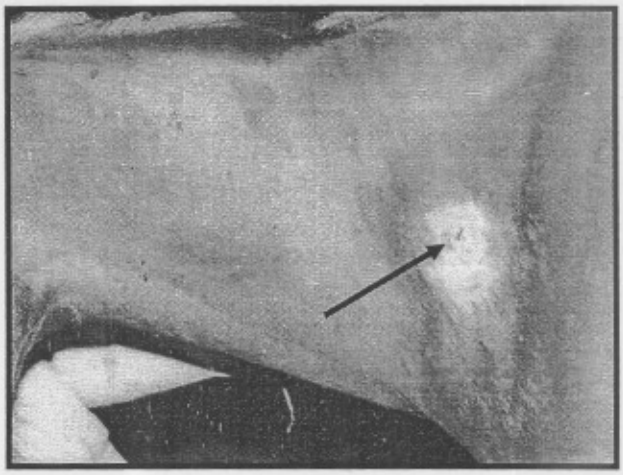

Fig. 3:Ulcer at the lateral aspect of the neck of a horse after subcutaneous injection of Ultrabac vaccine

Fig. 4: Swelling with small wound at the lateral aspect of the neck of a mule after intramuscular injection of phenylbutazone (Butaphenyl)

Fig. 5: Phlegmone of the whole hind limb with multiple ulcerative wounds of a horse after intramuscular injection of Flunixine Meglumine (Finadyne) (lateral view).

Fig.6: The same picture of (5) while (posterior view)

Fig. 7: old ulcerative wound of the buttocks of a puppy after subcutaneous injection of Procaine adrenaline for tail docking.

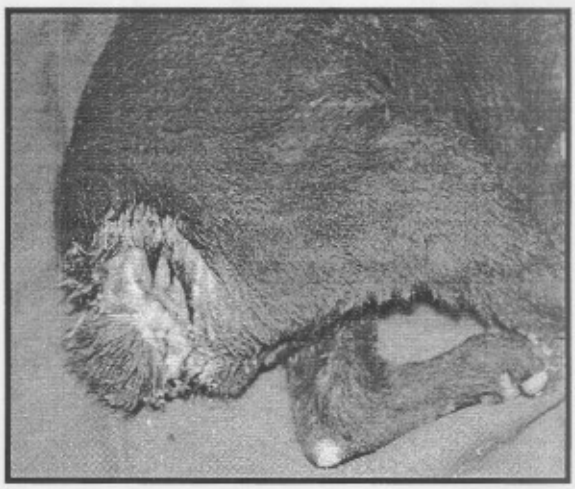

Fig.8: old ulcerative wound at the lateral aspect of the neck of a cow after subcutaneous injection of Ucimizole

Fig. 9:Old ulcerative wound at the lateral aspect of the neck with multiple fistulae and loosly attached skin at the pectoral region of a horse after subcutaneous injection of Ucimizole

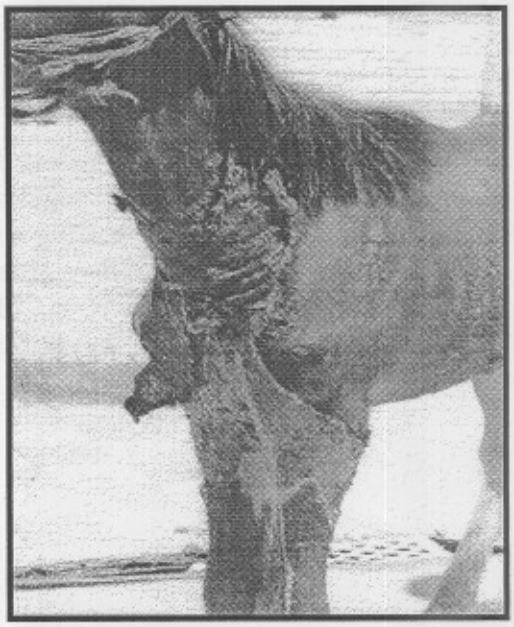

Fig. 10: Massive sloughing of the skin at the ventral aspect of the neck and pectoral region of a horse after subcutaneous injection of Ivomec

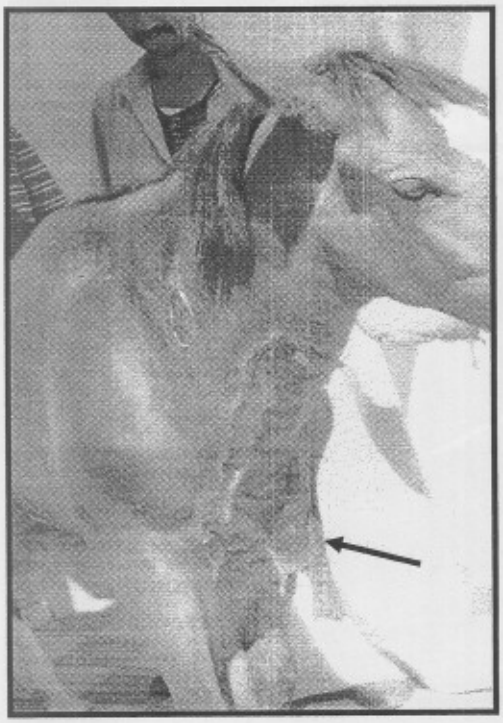

Fig. 11: Massive sloughing of the skin at the ventral aspect of the neck and pectoral region (black arrow) in addition to the site of injection (white arrow) of a horse after subcutaneous injection of Ivomec

Fig. 12: The same picture in (11) after one week of treatment and initiation of the healing by second intention observing of healthy granulation tissue in wound.

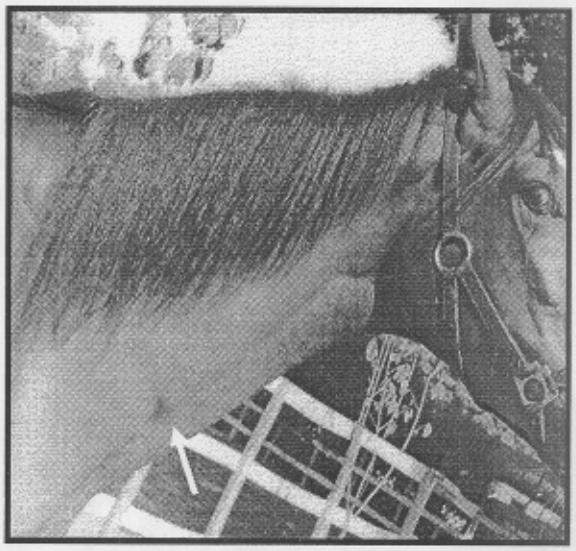

Fig. 13: Fibrotic myopathy manifested by depression at the jugular furrow as a result of healing of myonecrosis observed after default injection of phenylbutazone in a horse (arrow)

Fig. 14: Complete healing of open wound at picture (8), after one months of treatment by unnoticed scar tissue (arrow)

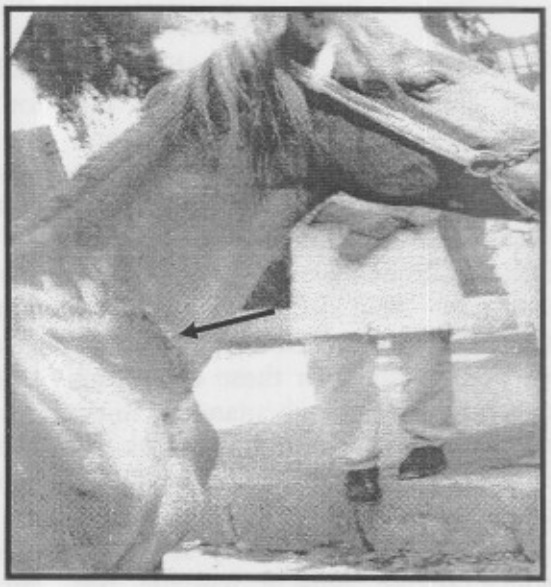

Fig. 15: Complete healing of open wound at picture (9), after one months of treatment, notice scar tissue (arrow)

Fig. 16: Complete healing of open wound at picture (11&12), after two months of treatment, notice large scar tissue (arrow)

DISCUSSION

In this study, the complications resulted from and at the site of drug injection in animals were discussed. Different animals were affected, and commonly equine species. It may due to the caustic and irritant effect of these drugs in equine *(16,23)* However the limited number of drugs used in equine in veterinary field in Egypt allowed to this misused of drugs. There was no breed, age and sex predilections for these conditions *(16,17)*. Intramuscular and subcutaneous injection were the recorded route and the neck and gluteal region were the common site of injection in this study. Intramuscular administration of the veterinary drugs especially in the gluteal can induce severe muscle damage resulting in economic losses and residue persistence *(18,23,24)*.

The signs met with the recorded cases that ranged from small localized swelling at the site of injection to massive necrosis and sloughing of skin and subcutaneous tissues; were not reflecting to the sensitivity reactions of drugs (drug eruption). Drug eruption can mimic virtually a dermatosis (e.g., urticaria, popular dermatitis, generalized pruritis or vesicular dermatitis) *(2,16)*. The clinical symptoms may result from the escharotic drugs, incorrect dose or route of drug administration, using of drug in non-indicated animal species or introduced infection with injection.

From the pamphlet of these drugs Pentomycin, Terramycin LA, Ultrabac vaccine, Levamizole 10% and Ivomec were not injected in equine. Ucimizole was not injected by overdoses in equine. The dosage of levamizole was not injected at one site in cattle while the complications observed in this study denote to the dose was injected wholly at one site. Imizol must be intramuscularly injected in equine and Butaphenyl & Finadyne must be intravenously injected. In this study injection was administered S/C with Imizol, S/C & I/M with Butaphenyl and I/M with Finadyne. The observed surgical disorders were also recorded with administrations of Pencillin & Streptomycin, Oxytetracycline, Phenylbutazone, vaccines, Levamizole and Ivermectin *(12,14,18,20,25)*. The drawback observed at the proximal part of the tail extended to the hindquarters was due to effect of vasoconstrictors in delicate skin and appendages *(21,22)*. Myonecrosis and skin sloughing resulted following I/M or inadvertent perivascular administration may be due to infections from contaminated injections *(1-3,5-11)*.

Cellulitis, abscess, phlegmone, myonecrosis and skin sloughing were the common clinical findings recorded following and at the site of injection *(1,3,16,23)*.

Diffuse cellulitis calls for aggressive antibiotic therapy and close observation of abscess formation. Surgical fenestration, debridement, lavaging with antiseptics and local antibiotics were used as the methods for opened wounds treatment *(3,4,9,23,26)*). Wounds resulted in these conditions were old, contaminated and had a considerable or massive skin loss. Therefore, suturing was impossible and the wounds were commonly managed by wound contraction and epithelialization. The initial goal of second intention healing is complete filling or covering of the wound with healthy granulation tissue. Granulation tissue prevents wound infection, promotes wound contraction, provides scaffold for epithelial cells to cover the skin defect *(27-29)*.

Outcome was good in all cases. Healing was attempted by second intention. The fate of these affections resulted either a firm dense scar tissue near the muscle (fibrotic myopathy) or scar tissue formation in the skin. The majority of fibrotic myopathy and scar formation were depended onto the size of soft tissue destruction *(28,30,31)*.

Lastly it was recommended that; increase the number of drugs used in equine through the pharmaceutical companies In addition to the use of each drug is through its specific route and in its specific animal species. The pamphlet of drugs must be applied. Intravenous injection is the prime route and the intramuscular injection must be given in the cervical muscles. Multiple injection is

avoided at one area and strictly aseptic precautions in injections (needle, syringe, drugs and site of injection) must be put in consideration.

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الملخص العربي

العناية الجراحية لموات العضلات وانسلاخ الجلد نتيجة أخطاء في حقن الأدوية

أحمد السيد بحيرى

قسم الجراحة كلية الطب البيطري جامعة الزقازيق

أجريت هذه الدراسة على خمسة وثلاثون حيوان من مختلف الفصائل (خمسة وعشرون من الفصيلة الخيلية وثمانية من البقر و كلبين) وردت إلى قسم الجراحة كلية الطب البيطري جامعة الزقازيق خلال خمسة سنوات من الفترة (٢٠٠٢-٢٠٠٧)٠ تراوحت أعمار الحيوانات المصابة من شهرين إلى تسع سنوات٠ وكانت هذه الحيوانات تعانى من إصابات جراحية نتيجة حقن الأدوية الآتية: مركب البنسلين مع الاستربتومايسين (بنتومايسين-شركة يونيفت-ايرلندا) و أوكسيتتراسيكلين (شركة النصربمصر) و تيراميسين طويل المفعول (شركة فايزر) عن طريق العضل فى الخيول وكذلك اميزول (شركة شيرنج) و لقاح الترباك (فايزر) عن طريق حقنهم تحت الجلد في الخيول وأيضا فينيلبيوتازون (بيوتافينيل- شركة يونيفت-ايرلندا) عن طريق العضل وتحت الجلد في مختلف الحيوانات المذكورة ، فلونكسين مجليومين (فينادين- شركة شيرنج) و كافوزال (شركة الإسكندرية بمصر) عن طريق العضل في الخيول ، بروكايين أدرينالين تحت الجلد في كلب ،ليفاميسول (شركة ممفيس بمصر)، يوسىميزول (شركة أمون) عن طريق حقنهم تحت الجلد في البقر والخيول و أيفرمكتين (أيفوماك) تحت الجلد في الخيول٠ حقنت هذه الأدوية لفتح الشهية و كوقاية من الميكروبات والطفيليات هذا بالإضافة لعلاج العرج وقطع الذيل في كلب٠ تبين أن معظم حقن الأدوية كان في العضل وخاصة في عضلتي الرقبة والالية٠

قسمت الإصابات التي ظهرت في مكان الحقن بعد حقن الأدوية بثلاث إلى خمسة أيام إلى خمسة أنواع بناءا على الأعراض الإكلينيكية (التهاب النسيج الخلوي-خراج-التهاب قيحى منتشر-موات في العضلات و انسلاخ الجلد)٠ تم علاج كل نوع من الإصابات بعلاجها المناسب٠ وتم شفاء كل الحالات ٠ نتج عن التئام الجروح ندبة ليفية في العضلات والجلد ٠

أظهرت هذه الدراسة بعض التوصيات و هي: زيادة عدد الأدوية المستخدمة في الخيول من الشركات المختلفة، استخدام كل دواء في مكانه والحيوان المخصص لاستخدامه، ضرورة إتباع تعليمات نشرة كل دواء، الحقن الوريدي هو الأفضل وان كان ضرورة للحقن العضلي فيفضل عضلات الرقبة، تجنب تكرار الحقن في موضع واحد و لابد من ضرورة الاحتياطات الأزمة للتعقيم عند الحقن من(إبرة، سرنجة، دواء و مكان الحقن)٠