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Brief Communication

TISSUE DAMAGE AT THE INJECTION SITE AFTER INTRAMUSCULAR INJECTION OF DRUG PREPARATIONS FORMULATED BY ADDITION OF POLYVINYL-PYRROLIDONE

During the last years a number of papers have been published describing tissue damage at the injection site in various animals after intramuscular injection of preparations containing antibiotics and chemotherapeutics (vide *Rasmussen & Svendsen* 1975). Further, it has been published that addition of polyvinylpyrrolidone (PVP, Plasdone C-15) to preparations containing oxytetracycline should diminish or even prevent the irritating effect at the injection site (*Weber & Molenaar* 1971). The purpose of the present study was to examine the effect of PVP in preparations containing oxytetracycline and sulphadimidine. For the experiments were used 12 swine weighing 40—110 kg. The preparations used and the number of injection sites are listed in Table 1. The volume administered intramuscularly in the neck, the back or the thigh was in all cases 10 ml. The animals were killed 6 to 14 days after the injections. The injection sites were excised for macroscopic and microscopic examinations immediately after killing (vide *Rasmussen & Svendsen*).

Terramycin vet.® 5 % and 10 %

Six days after intramuscular injection of Terramycin vet.® 5 % and Terramycin vet.® 10 % containing 17.5 % PVP no differences could be observed. In both series pocket formations with yellow-brown discolouration and sero-fibrinous exudation were seen in the subcutaneous tissue. The muscle tissue was grey with bleedings. In most of these cases necroses were found (from a few mm and up to $5 \times 2 \times 2$ cm) surrounded by a haemorrhagic demarcating zone as earlier demonstrated in cows and swine (*Rasmussen & Høgh* 1971).

The histological examinations showed in all cases hyaline degeneration and in most cases necrosis of the muscle fibres. The necroses were surrounded by demarcating zone with proliferated fibroblasts and histiocytes, furthermore sero-fibrinous exudation and oedema were seen.

Fourteen days after the injection of Terramycin vet.® 5 % 4 out of 5 injection sites were found affected. In the case of

T a b l e 1. Affected area and histological findings at the injection site 6 and 14 days after intramuscular injections of various preparations.

Preparations	Days after the injection	Number of injection sites	Number of injection sites affected	Size of affected area cm min.-max.
Terramycin vet.® 5 %, Pfizer	6	5	5	6×1×1.5 15×12×5
	14	5	4	1×0.5×0.5 10×6×5
Terramycin vet.® 10 %, Pfizer (containing 17.5 % PVP)	6	17	17	1×0.5×0.5 10×3×3
	14	11	6	1×0.5×0.5 15×6×1
Inj. sulphadimidini 0.2 g/ml Ph.N. 1964	6	5	5	12×2×1 10×7×3
	14	5	5	2×2×1 12×4×4
Inj. sulphadimidini 0.2 g/ml Ph.N. 1964 (added 22 % PVP)	6	8	8	8×2×1.5 10×4×3
	14	5	5	5×2×1 10×3×2

Terramycin vet.® 5 % and Terramycin vet.® 10 % are kindly supplied by Pfizer A/S, Copenhagen. Polyvinylpyrrolidone is kindly supplied by GAF A/S, Copenhagen.

Terramycin vet.® 10 % containing PVP only 6 out of 11 injection sites were found affected (Table 1). The affected areas were smaller than at day 6 but it was still possible to see necroses, haemorrhagic demarcating zones and discolourations. The histological picture was very much similar to that at day 6 without the sero-fibrinous exudation and oedema. Only few calcifications and polynuclear giant cells were seen.

Inj. sulphadimidini 0.2 g/ml and inj. sulphadimidini 0.2 g/ml added PVP.

Six and 14 days after intramuscular injection of preparations containing sulphadimidine and sulphadimidine added 22 % PVP no differences in tissue reactions could be observed. At all injection sites necroses and tissue reactions were seen similar to those seen earlier (*Rasmussen et al.* 1973).

The histological examination showed the same reactions as described after injection of oxytetracycline but the number of polynuclear giant cells and calcifications were much more pro-

nounced especially at day 14 and thus similar to earlier findings in swine (*Rasmussen et al.*).

Sulphadimidine was found at all injection sites at day 6 (0.3—10 µg/g) and at day 14 (0.3—0.8 µg/g).

Conclusion

At day 6 it was not possible to demonstrate any differences in tissue reactions to Terramycin vet.® 5 % and Terramycin vet.® 10 % containing 17.5 % PVP. However, at day 14 a relatively smaller number of injection sites was found affected after injection of Terramycin vet.® 10 % containing PVP than after injection of Terramycin vet.® 5 %. Addition of 22 % PVP to the alkaline inj. sulphadimidini 0.2 g/ml did not diminish the tissue damaging effect after intramuscular injection.

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