

Pharmacological alternatives to oxytetracycline as potential treatment of flexural limb deformities in foals

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Introduction

Flexural limb deformities are a widespread condition in foals. Oxytetracycline is a common conservative treatment option due to its relaxing effect on the muscle-tendon unit, potentially mediated by inhibition of matrix metalloproteinase (MMP) activity (1; 2; 3; 4). However, its antimicrobial properties and potential adverse side effects warrant the investigation of alternatives. In this study, the influence of a panel of substances, with potentially similar mechanisms of action on flexural deformities, however without antimicrobial properties, on the viability and proliferation of juvenile tendon myofibroblasts, as well as on collagen gel contraction, was assessed *in vitro*.

Materials and Methods

Myofibroblasts from forelimb SDFTs and accessory ligaments of the DDFTs from 6 foals, euthanized for reasons unrelated to this study, were cultured and characterized by immunohistochemistry. The myofibroblasts were incubated with oxytetracycline, the MMP-inhibitors incyclinide, ilomastat, aprotinin and pentoxifylline, the lathyrogenic agent β -aminopropionitrile fumarate (BAPN) and Dulbecco's modified Eagle medium (DMEM) as control. Viability and proliferation capacities of the myofibroblasts were assessed through colorimetric cell viability (MTS) and crystal violet assays. Moreover, the cultured myofibroblasts were seeded in collagen gels containing oxytetracycline, the aforementioned potential alternative substances and DMEM. The gel surface areas were measured on photographs at 2, 4, 6, 8, 24, 48, 72, and 96 hours after release. Contraction differences between gels incubated with the various substances were statistically evaluated using a mixed-model analysis of variance.

Results

The morphology and immunohistochemistry profile of the cultured cells were consistent with tendon and ligament myofibroblasts. All test substances were biocompatible (no cytotoxic or anti-proliferative effects), as shown by the absence of significant differences in cell viability between cells incubated with the test substances and DMEM. Compared to DMEM, BAPN, incyclinide, and ilomastat induced a significant inhibition ($p < 0.05$) of collagen gel contraction by myofibroblasts at all time points, except at 2 hours for ilomastat. The inhibition was significantly more potent than that observed with oxytetracycline as of 8 hours.

Discussion and Conclusion

At the tested concentrations, none of the substances had a negative impact on the viability or proliferation capacity of cultured juvenile myofibroblasts (5). BAPN, incyclinide, and ilomastat demonstrated a significant inhibitory capacity on collagen gel contraction by myofibroblasts, representing the tendinous part of foals' muscle-tendon unit. This underscores their potential as substitutes for oxytetracycline. Further investigations are needed to elaborate on their potential side effects, pharmacodynamics, pharmacokinetics, and application methods in juvenile equine patients before these promising *in vitro* findings can be translated into *in vivo* applications.

References

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