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Treatment for Mucopolysaccharidosis Type VI in Cats

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Perspective Article

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INTRODUCTION

Mucopolysaccharidosis type VI (MPS VI), familiarly known as Maroteaux-Lamy syndrome, occurs due to the deficiency of the lysosomal hydrolase N-acetylgalactosamine 4-sulfatasewhich is a progressive condition that causes many tissues and organs to enlarge, become inflamed or scarred, and eventually causing atrophy, due to which production or functioning of lysosomal enzymes required for digestion of Glycosaminoglycans (GAGs). Fibroblast-mediated ex vivo gene therapy and Enzyme Replacement Therapy was evaluated in the N-acetylgalactosamine 4-sulfatase (4S) deficient Mucopolysaccharidosis type VI (MPS VI) in cats. Cats suffering from IDUA deficiency experience various difficulties such as bone and joint deformity, upper airway obstruction, hepatosplenomegaly, cornea clouding and cognitive impairment.

ABOUT THE STUDY

In a feline model of mucopolysaccharidosis type VI administration of feline N-acetylgalactosamine-4-sulfatase (rf4S) seems to be effective in reducing urinary glycosaminoglycan levels and lysosomal storage according to the previous studies. In this study, we aim to elaborate utilization of enzyme replacement therapy proving to have high efficacy and advantageous. 4S gene-transduced skin fibroblasts were implanted under the renal capsule of MPS VI cats. This method was initially developed in nude mice and involved implanting clonal populations of rabbit fibroblasts expressing human growth hormone under the renal capsule. Low levels of 4S activity were detected in peripheral blood leukocytes from cats 241, 244 and 246 shortly after implantation of autologous, gene-corrected fibroblasts but were no longer detectable after 3–8 weeks post-implantation. When intravenous dose of 4S was administered, low levels of 4S activity were detected in peripheral blood leukocytes. Gross pathology and radiological assessment techniques can be used to evaluate disease progression in these cats, providing information about disease progression. However, implantation of autologous gene-transduced fibroblasts under the renal capsule is associated with significant risk of mortality. The life expectancy of the affected cats depends on the severity of the disease and is generally reduced due to respiratory, neurodegenerative and intestinal abnormalities.

Symptoms and diagnosis

The disease is characterized by distinct enzymatic deficiencies and genetic mutations like MPS I, MPS VI and MPS VII, coinciding with human cases of Hurler syndrome, Maroteaux-Lamy syndrome and Sly syndrome. Diagnosis is usually conducted through clinical examination, urine tests and enzyme assays.

Treatment

Gene delivery method offers many advantages, because using cells as vectors can permit the manipulation and control of many steps that occur in vivo with direct delivery. Dose responsive effect of ERT, with clear improvement at 1 mg/kg and greatest effect at 5 mg/kg. ERT was effective in reducing development of soft tissue and skeletal pathology, correlating well with improvements. The 0.2-mg/kg dose appeared insufficient to significantly alter progression of soft tissue and skeletal disease. Evaluation of the effects of gene therapy can be carried using repeated-measure ANOVA (Analysis of Variance).

CONCLUSION

It is feasible to use lower doses of same-species enzyme to achieve the same efficacy of therapy as a higher dose of non-species-specific enzyme. Comparatively ERT from birth at 1 and 5 mg/kg rh4S was shown to be very effective at reducing development of pathology in all tissues examined except cartilage and cornea, with the greatest effect seen at 5 mg/kg than Fibroblast-mediated gene therapy. Several treatment options are still being developed, and an affected cat's life expectancy and quality largely depend on the severity of the disease. The safest measures against mucopolysaccharidosis in cats are in preventing the succession of the genetic mutation through generations.