Abstract

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Ascorbate regulation of collagen biosynthesis in Ehlers-Danlos syndrome, type VI.

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OBJECTIVE: We studied two unrelated individuals with Ehlers-Danlos syndrome type VI, which is characterized by congenital hypotonia, lax joints, severe kyphoscoliosis, friable skin, and hemorrhagic hypotrophic scars. The diagnosis was confirmed by decreased hydroxylysine residues in dermal collagen and decreased collagen lysyl hydroxylase activities in their cultured skin fibroblasts.

METHODS AND RESULTS: Despite the diminished hydroxylysine residues in dermal collagen from the probands, we found no differences in hydroxylysyl residues of collagen synthesized by fibroblasts in culture. When patient 1 was given oral sodium ascorbate (5 g/d) for 3 weeks, ascorbate concentrations increased two-fold in plasma and 300-fold in urine. Urinary excretion of hydroxylysine and hydroxyproline increased during ascorbate administration. After a 1-year interval, bleeding time, wound healing, and muscle strength improved. Ascorbate supplementation (50 micrograms/mL) to confluent fibroblasts cultured from the two patients and controls increased hydroxyprolyl and hydroxylysyl residues of fibroblasts four to seven and three to four-fold respectively. Total protein associated with the cell layer increased 14% to 32% without concomitant change in cellular DNA. Total soluble collagenous material recovered from culture media increased 61% to 103% with ascorbate supplementation.

CONCLUSION: These studies demonstrate that ascorbate improves the clinical status of patients with impaired collagen lysyl hydroxylase activity by enhancing lysyl and prolyl hydroxylation and total collagen production.

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