REDUCED BIOMECHANICAL STRENGTH OF THE THORACIC AORTA IN THE OIM (OSTEOGENESIS IMPERFECTA MODEL) MOUSE.

Charlotte L Phillips, Angela G. Vouyouka, Brent J. Pfeiffer, Timothy A. Taylor. University of Missouri - Columbia, Columbia, Missouri, U.S.A.

Type I collagen is normally a heterotrimer of two pro alpha1(I) collagen chains and one pro alpha2(I) collagen chain. Mutations in either the pro alpha1(I) and pro alpha2(I) collagen genes can result in osteogenesis imperfecta (OI). Ol is classified into four types (Sillence types I-IV) based on the mode of inheritance and severity of the skeletal, ocular, otologic, and dental abnormalities. The extra-skeletal effects of Ol on the vasculature are less well understood; these include vessel fragility, aortic root dilatation (in an estimated 12.1% of Ol patients, Hortop et al., Circulation 73:54, 1986), aortic and/or mitral insufficiency, and aortic dissection. Objectives: The goal of this study was to evaluate the biomechanical properties of the thoracic aorta using an Ol murine model (osteogenesis imperfecta model: oim). The oim/oim mice have phenotypic features similar to type III Ol as a result of homozygosity for a null mutation in their pro alpha2(I) collagen genes [preventing formation of normal heterotrimeric collagen; resulting in only homotrirneric type I collagen, alpha1(I)3, synthesis (Chipman et al., PNAS, 90:1701, 1993)]. The heterozygous mice, oim/+, exhibit features similar to mild Ol (Saban et al., Bone 19:575, 1996). Methods: Seven oim/oim, seven oim/+, and six wildtype, +/+, mice were euthanized by CO2 asphyxiation. The thoracic aorta was harvested and 5 mm rings prepared from the ascending and descending portion. Load-xtension curves were obtained using a stretching apparatus for each ring in Krebs solution at room temperature. Ultimate tensile load Fmax) and incremental elastic modulus (IEM) were standardized per dry mass of specimen and mean values among groups were compared using ANOVA. Results: The ascending aorta in oimloim mice suggested a trend toward lower Fmax and EIM (Fmax= 133 +/- 43 g/mg, EIM= 233 +/-135 g/mg/mm) as compared to oim/+ (Fmax= 180 +/- 72 g/mg, EIM= 210 +/- 80 g/mg,mm) and +/+ (Fmax= 229 +/-94 g/mg, IEM= 416 +/-260 g/mg/mm, p= 0.1). This reduction in biomechanical strength was statistically confirmed in experiments evaluating the descending aorta and demonstrating values of lower Fmax (p= 0.00002) and IEM (p= 0.0006) in oim/oim (Fmax= 133 +/-90 g/mg, IEM= 148 +/-66 g/mg/mm) as compared to oim/+ (Fmax= 294 +/- 99 g/mg, 543 +/-232 g/mg/mm) and +/+ (Fmax= 397 +/- 110 g/mg, IEM= 858 +/- 215 g/mg/mm). Conclusion: Oim/oim mice have significantly weaker and more extensible aorta as compared to normal litteraates. Heterozygous (oiml+) mice express similar patterns of aortic biomechanical deficiency, but to a lesser degree.

Reference: Proceedings of the 7th International Conference on Osteogenesis Imperfecta. Montreal, Canada, 1999.