URINARY LEVELS OF COLLAGEN DEGRADATION PRODUCTS SUGGEST THAT BONE RESORPTION IS NORMAL IN CHILDREN WITH OSTEOGENESIS IMPERFECTA.

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Bone metabolism is characterized by two opposite processes: the formation of new bone by osteoblasts and the degradation or resorption of old bone by osteoclasts. Since one of the features of osteogenesis imperfecta (OI) is osteoporosis, the balance between bone formation and resorption must be disturbed. Bone is the primary store of collagen type I in the body and is believed to remodel faster than most major connective tissues. Thus, biochemical tests assessing collagen metabolism can be used as markers of bone formation and bone resorption. Serum concentrations of either the C-terminal or N-terminal propeptide of procollagen I (PICP or PINP), markers of bone formation, have consistently been reported to be lower in OI children compared to age-matched healthy controls, indicating a reduced production of collagen type I [1-5]. There are contradicting reports with respect to markers of bone resorption. The urinary excretion of type I collagen crosslinked N-telopeptides (NTx) was reported to be elevated in OI children [6], whereas the serum concentration of type I cross-linked C-telopeptides (ICTP) was reported to be lower compared to age-related controls [1]. Finally, urinary levels of hydroxyproline (Hyp) and the crosslinks hydroxylysylpyridinoline (HP) and lysylpyridinoline (LP) in OI children were reported to be the same as in healthy controls [1,4,5,7,8]. We have investigated Hyp, HP, LP, NTx as well as galactosylhydroxylysine (GH) and glucosylgalactosylhydroxylysine (GGH) levels in urine of 41 OI patients (age 3-17 years) and compared them to 72 healthy controls (age 1-18 years). All markers were normalized to urinary creatinine levels. In OI, levels of all markers were within the range as found for the control group, indicating that the rate of bone resorption in OI is normal. It thus seems that the osteoporotic status in OI is mainly the result of a decreased collagen synthesis. Interestingly, the ratio of urinary Hyp to HP and LP was comparable with that of controls, indicating a normal collagen cross-linking in OI bone. The direct measurement of the pyridinoline cross-link level (HP+LP) in bone of 27 OI patients (2-15 years) revealed a normal level indeed. Another unexpected finding is, that there are no differences in the ratio of urinary Hyp to GH+GGH in OI patients and normal subjects. From this we conclude that the glycosylation level of collagen in OI bone is normal as well. We are currently investigating this remarkable finding in more detail.

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