APD - TREATMENT IN OSTEOGENESIS IMPERFECTA.

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Purpose
We reported the first case of intravenous APD-treatment in OI at the Fifth International conference on OI in 1993. Three years later we reported promising results in three adolescents with severe OI. Now we have positive results in a larger group during one to eight years of treatment.

Patients
Sixteen patients with OI aged 1 to 20 years at the start of treatment. The severity of their condition varies from severe forms with multiple fractures, daily pain from the skeleton and short stature to milder forms with fractures and compression of the spine.

Methods
The patients were treated with APD as monthly infusions of 10-30 mg/m² for one to eight years. The intravenous route was chosen to prevent differences in bioavailability from interfering with the interpretation of results. To avoid negative side effects as fever and muscular pain, the APD-infusion was given slowly, after hydration. To compensate for a generalized decrease in serum Ca levels almost all patients needed an additional oral daily treatment with 0,25 ug of 1.25-dihydroxycholecalciferol. Bone turnover was assayed every six month by determination of serum Osteocalcin, ALP (alkaline phosphatase), P1CP, 1CTP, Ca, PO4, PTH and urinary Ca/creatinine quote. ALP including isoenzymes was determined by HPLC (high performance liquid chromatography), P1CP and 1CTP by RIA and Osteocalcin by IRMA (immuno radiometric assay). In other tests standard techniques were used.
Bone density was determined by DEXA measurements, of the total body and spine.
Pain and daily activities were estimated and a record was kept by the patients or parents in special diaries on a 10-degree scale.

Results
In all sixteen patients DEXA measurements every six month showed a successive increase in bone density. All variables showed continuos decrease in bone turnover during the time of treatment.
For the younger patients scores of pain, well-being and activities of daily life greatly improved. No negative side effects were observed.

Conclusions
In the absence of curative treatment of OI, APD seams to be an efficient symptomatic treatment without negative side effects. Our results suggest that the beneficial effect is more pronounced in growing persons with a high bone turnover. An important issue is to compare different studies and discuss doses and their intervals, to find the optimal treatment that interferes as little as possible with the patients normal life.

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