Spinal complications in osteogenesis imperfecta

47 patients 1–16 years of age

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We examined in a cross-sectional study, 47 children (mean age 7.7 (1–16) years) with osteogenesis imperfecta (OI) to find the prevalence of spinal deformities and to correlate these observations with anthropometry. The associations between dentinogenesis imperfecta, joint hypermobility and spinal deformities were also studied.

Disproportion in stature in OI type I and type IV was mainly caused by spinal involvement, as evidenced by a greater decrease in body height than in leg length. In OI type I, the decrease in sitting height was mainly caused by platyspondyly, whereas in OI types III and IV, it was also caused by progressive scoliosis and kyphosis. Scoliosis was present in 22 children, and pathological kyphosis in 18, mainly in the severe OI types. Basilar impression was observed in 10 children, mainly in type III.

Children with dentinogenesis imperfecta seemed to be prone to develop scoliosis, pathological kyphosis and basilar impression. Children with generalized joint hypermobility were less prone to develop scoliosis and basilar impression. Our observations may contribute to a better understanding of the risk factors for progressive spinal deformities in OI.

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Major clinical characteristics of OI are osteopenia and fragility of bone, variable degrees of short stature and progressive skeletal deformities. Data regarding spinal deformities in childhood are scarce and have been reported to be between 11% and 92%, depending on the system of classification used (King and Bobechko 1971, Falvo et al. 1974, Hoek 1975, Benson et al. 1978, Ishikawa et al. 1996). Patients with the severest types of OI had a higher incidence of scoliosis.

We assessed the prevalence of spinal deformities and basilar impression in 47 children with OI and correlated these observations with anthropometry. The associations between the presence of dentinogenesis imperfecta, joint hypermobility and spinal deformities were also studied.

Children and methods

In a cross-sectional study, we examined 47 children with OI, who regularly attended the Wilhelmina Children's Hospital, which is a national referral center for the treatment of children with OI. These children are a representative sample of children with this condition. Mean age of the study population was 7.7 (1–15) years. We divided our patients into 6 types (IA, IB, II, III, IVA and IVB) (Sillence et al. 1979, Sillence 1994). Height, sitting height, leg length and head circumferences were measured in a standardized way and compared to reference values for Dutch children (Gerver et al. 1989). Generalized hypermobility of the joints was determined according to Bulbena et al. (1992). Dentinogenesis imperfecta was diagnosed, if the teeth were opalescent, discolored or fragile. If the presence of dentinogenesis imperfecta was doubtful, microscopic examination of the deciduous teeth was performed.

Spinal radiographs were taken in all children and measurements were obtained regarding the presence, localization and severity of scoliosis (Cobb 1948). Scoliosis of 10° or more and kyphosis of more than 40° or less than 10° were considered pathological (Propst-Proctor and Beck 1983). The lateral radiograph of the spine was mainly used to determine the location of platyspondyly and biconcave vertebrae. Basilar impression was measured on a plain lateral

Table 1. Patient characteristics related to the various types of osteogenesis imperfecta

	OI type I (n 17)	OI type III (n 16)	OI type IV (n 14)
Mean age, years	6.8	7.3	9.5
range	1–15	2–12	2–15
Boys/girls, n	5/12	8/8	9/5
Joint hypermobility, n	15	0	1
Dentinogenesis imperfecta, n	4	14	3
Scoliosis, n	2	10	10
Mean Cobb angle (°)	5	18	17
range	0–20	0–60	0–46
Kyphosis, n	4	10	3
Mean Cobb angle (°)	21	29	30
range	0–52	-10–55	-10–48
Location of platyspondyly, n			
entire spine	3	15	6
thoracal	0	0	2
lumbar	3	0	2
thoraco-lumbar	2	1 2	
Basilar impression	0	7	1

skull radiograph in 42 children, using the McGregor line in relation to the position of the odontoid and it was confirmed by MRI when positive or doubtful on the radiograph (McGregor 1948).

Statistics

Anthropometric measurements were transformed into Z-scores, which were related to an external reference population (Gerver et al. 1989). Data within 2 standard deviations were considered normal. Z-scores were compared with the Student's t-test. The association of categorical variables was expressed as an odds ratio. The odds ratio can be viewed as a relative risk. For example, an odds ratio of 2.0 for pathologic kyphosis in children with scoliosis means that the risk of having pathological kyphosis is twie as great in children with scoliosis as in children without scoliosis.

Comparison of categorical variables was calculated with chi-square analysis. A p-value of < 0.05 was considered significant.

Results

17 children had OI type I, 16 had type III and 14 had type IV (Table 1). 16 children (34%), 15 of them with OI type I, were classified as having generalized hypermobility.

Dentinogenesis imperfecta (DI) was present in 21 children. In type I, DI was found in 4 children wheras DI was uncertain in 2 children. DI was present in 14 children with type III and was uncertain in 1 child. DI was observed in 3 children with type IV, whereas in 1 child the presence of DI was uncertain. In a 2-year-old child, DI could not be evaluated because no primary dentition was present.

Scoliosis

22 children had scoliosis of 10° or more, mainly those with type III or IV. A double curve scoliosis developed in 9 children with OI types III and IV.

In the 13 children younger than 5 years of age, scoliosis was detected in 2 children with type III and in 3 children with type IV. In the 13 children older than 5 years of age, scoliosis was found in 2 children with type I, in 8 with type III and in 7 with type IV. No significant relation between age and the presence of scoliosis was present ($p = 0.3$).

Kyphosis

17 children had pathological kyphosis. 9 children had kyphosis of more than 40° (type I: 1, type III: 6, type IV: 2). 9 children had kyphosis of less than 10° (type I: 1, type III: 6, type IV: 2). There was no relation between age and the presence of pathological kyphosis ($p = 0.3$).

Platyspondyly

36 children had wedge-shaped or biconcave vertebrae (platyspondyly) (Table 1). The entire spine was involved in 24 children, mainly in type III. 12 children had local involvement of the spine, especially in the lumbar and thoracolumbar regions, mainly in types I and IV.

Basilar impression

8 children had a basilar impression and were older than children with no basilar impression ($p = 0.002$). There was no significant relation between the Z-score of the head circumference and the presence of basilar impression ($p = 0.9$).

Anthropometry

In type I children, the mean Z-score for height was –1.6 (SD 1.3). Decreased height was mainly caused by a decrease in sitting height, rather than in leg length (mean Z-score sitting height: –3.4 (1.0), mean Z-score leg length: 0.5 (1.8)).

In type III children, mean Z-score for height was –8.0 (2.0). This was caused by almost equal decreases in sitting height and leg length (mean Z-score sitting height: –7.6 (2.1), mean Z-score leg length: –6.4 (2.1)).

In type IV children, the mean Z-score for height was –2.8 (1.7). Decreased height was mainly due to a decrease in sitting height (mean Z-score sitting height: –4.4 (1.6), mean Z-score leg length: –0.8 (1.8).

Table 2. Association of categorical variables in osteogenesis imperfecta (odds ratio and 95% confidence interval)

Variables	Odds ratio	95%CI
Hypermobility/dentinogenesis imperf.	0.3	0.05–1.3
Hypermobility/scoliosis	0.08	0.01–0.5
Hypermobility/kyphosis	0.2	0.04–1.2
Hypermobility/basilar impression	0	0–1.0
Dentinogenesis imperf./scoliosis	3.4	0.8–15.1
Dentinogenesis imperf./kyphosis	5.8	1.2–29.8
Dentinogenesis imperf./basilar impr.	infinite	
Scoliosis/kyphosis	2.1	0.6–8.3
Scoliosis/basilar impression	1.1	0.6–23.9
Kyphosis/basilar impression	3.5	0.6–23.3

Associations of clinical characteristics (Table 2)

Children with dentinogenesis imperfecta had scoliosis, pathological kyphosis and especially basilar impression more frequently and generalized hypermobility of the joints less frequently. Basilar impression was more commonly associated with kyphosis than with scoliosis. Children having scoliosis ran twice the risk of also having pathological kyphosis. Children with generalized joint hypermobility had a lower incidence of scoliosis and pathological kyphosis. No children with basilar impression had generalized hypermobility.

Discussion

Benson and Newman (1981) stated that scoliosis in OI was rare before the age of 6 years. After this age, a rapid progression of a scoliotic deformity occurred. Hanscom et al. (1992) described the natural history of spinal deformities in OI. They classified spinal deformities radiologically and divided OI into types A to E, depending on the degree of severity. They concluded that the natural history of scoliosis in patients who had types B, C, D or E was progression of the curve.

We observed that basilar impression in OI types III and IV children was closely linked to the presence of dentinogenesis imperfecta. Sillence (1994) reported the highest frequency of basilar impression in types IB and IVB where dentinogenesis imperfecta was also present. He suggested possible explanations for the presence of basilar impression in type IV patients. Besides greater osseous plasticity in OI type IV, he thought an earlier upright posture or sitting position in these children might afect the initiation of basilar impression. Charnas and Marini (1993) observed basilar invagination in 8 of 76 patients with types III and IV. Of these 8 persons, 5 were children.

Benson and Newman (1981) stated that the laxity of spinal ligaments reduces vertebral stability and allows for progressive spinal curvature. We found no association between generalized hypermobility and scoliosis. We believe that (micro)-fractures of the vertebrae cause wedge-shaped deformities and spinal collapse. We agree with Ishikawa et al. (1996), who concluded that the presence of 6 biconcave vertebrae or more before puberty indicated that a severe scoliosis of more than 50° was likely to develop. In our study, children with the severest types of OI had platyspondyly in almost the entire spine and had the most severe spinal deformities.

Our study showed that decreased height in types I and IV was primarily due to spinal involvement. These observations conflict with those of Beighton et al. (1983), who found trunk shortening in only 11 of 79 patients with OI type I. However, comparison is difficult because patients from 2 months to 69 years of age were included. Since the prevalence of OI is low, the accrual of large numbers of affected children occursonly in specialized referral centers. Our center has a bias towards younger children, because of its research focus on early intramedullary rodding and early ambulation. Therefore, comparison with studies concerning spinal involvement in OI is difficult, since most of these combined data about children and adults.

Wenstrup et al. (1990) reported 2 major biochemical phenotypes in OI. In one group, cells secreted about half the normal amount of normal type I procollagen and no identifiable abnormal molecules. These patients were generally of normal stature, rarely showed bone deformity or dentinogenesis imperfecta and had blue sclerae. In the other group, cells produced and secreted normal and abnormal type I procollagen molecules. Many such patients were short, had bone deformities and dentinogenesis imperfecta and had blue-grey sclerae. Most children in the first group had mild OI (type I), while in the other group more severe types of OI (types III and IV) were present. We used the classification of Sillence because collagen studies were not performed in all children.

We conclude that in children with OI types III and IV, with dentinogenesis imperfecta, progressive deformities such as platyspondyly, scoliosis, pathological kyphosis and basilar impression are more likely to occur than in children with type I.

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References

Beighton P, Spranger J, Versveld G. Skeletal complication in osteogenesis imperfecta; a review of 153 South African patients. S Afr Med J 1983; 64: 565-8.

Benson D R, Newman D C. The spine and surgical treatment in osteogenesis imperfecta. Clin Orthop 1981; 159: 147-53.

Benson D R, Donaldson D H, Millar E A. The spine in osteogenesis imperfecta. J Bone Joint Surg (Am) 1978; 60: 925-9.

Bulbena A, Duro J C, Porta M, Faus S, Vallescar R, Martin-Santos R. Clinical assessment of hypermobility of the joints: assembling criteria. J Rheumatol 1992; 19: 115-21.

Charnas L R, Marini J C. Communicating hydrocephalus, basilar invagination and other neurologic features in osteogenesis imperfecta. Neurology 1993; 43: 2603-8.

Cobb J R. Outline for the study of scoliosis. AAOS Instr Course Lect 1948; 5: 261.

Falvo K A, Root L, Bullough P G. Osteogenesis imperfecta: clinical evaluation and management. J Bone Joint Surg (Am) 1974; 56: 783-93.

Gerver W J M, Drayer N M, Schaafsma W. Reference values of anthropometric measurements in Dutch children. Acta Paediatr Scand 1989; 78: 307-13.

Hanscom D A, Winter R B, Lutter L, Lonstein J E, Bloom B, Bradford D S. Osteogenesis imperfecta; radiographic classification, natural history and treatment of spinal deformities. J Bone Joint Surg (Am) 1992; 74: 598-616.

Hoek K J. Scoliosis in osteogenesis imperfecta. Proceedings of the Western Orthopaedic Association. J Bone Joint Surg (Am) 1975; 57: 136.

Ishikawa S, Niigata-Shi S, Kumar J, Takahashi H E, Homma M. Vertebral collapse as a predictor of spinal deformity in osteogenesis imperfecta. J Bone Joint Surg (Am) 1996; 78: 212-9.

King J D, Bobechko W P. Osteogenesis imperfecta. J Bone Joint Surg (Br) 1971; 53: 72-89.

McGregor M. Significance of certain measurements of skull in the diagnosis of basilar impression. Br J Radiol 1948; 21: 171-81.

Propst-Proctor S L, Bleck E E. Radiographic determination of lordosis and kyphosis in normal and scoliotic children. J Pediatr Orthop 1983; 3: 344-6.

Sillence D O. Craniocervical abnormalities in osteogenesis imperfecta: genetic and molecular correlation. Pediatr Radiol 1994; 24: 427-30.

Sillence D O, Senn A, Danks D M. Genetic heterogeneity in osteogenesis imperfecta. J Med Genet 1979; 16: 101-16.

Wenstrup R J, Willing M C, Starman B J, Byers P H. Distinct biochemical phenotypes predict clinical severity in nonlethal variants of osteogenesis imperfecta. Am J Hum Genet 1990; 46: 975-82.