To the Editors:

Cyclical intravenous pamidronate therapy in children with osteogenesis imperfecta

Children affected with osteogenesis imperfecta (OI) have increased morbidity and mortality and no definite treatment has been found yet. Recurrent fractures and bone deformities are the main complications of this disease. Recent studies have shown the ability of intravenous pamidronate to prevent fractures, when given in a cyclical manner [1]. This treatment is being used currently to prevent recurrence of fractures in children with OI but the clinical experience with such therapy is greatly limited. In this brief communication, we report our experience in treating OI children with the intravenous pamidronate during the last 4 years.

Total of 28 children with age range of 21 days to 9 years were treated from August 2001 to December 2004. These patients were either direct admissions to paediatric units in Karapitiya Hospital or referred by paediatricians in other hospitals. All patients had suffered at least one fracture in either long bones or ribs before admission. The diagnosis of OI was made clinically by paediatricians in the team, and other metabolic bone diseases such as rickets and renal tubular acidosis were excluded by relevant biochemical tests. Parents were interviewed and benefits and complications of therapy were explained.

Children were treated with pamidronate sodium (Aradia by Novartis) 1.5–2.0 mg per kg bodyweight as an infusion in 1/5 isotonic saline over 6-hour period for three consecutive days. This was repeated every 3 months in cyclical manner until either the total bone mineral content (TBMC) became normal (defined as within 2 standard deviations from the mean TBMC of age and sex matched population) or for a maximum of 6 cycles. Children were kept under supervision during therapy for possible side-effects and open access was given to parents to report any unexpected side-effects. Serum calcium level was done at the end of each treatment session.

TBMC was assessed in 18 children by dual energy xray absorptiometry (DXA) using Norland Eclipse XR scanner (Norland Corp, USA). A rapid increase in TBMC was seen in all children, except one, during the period of treatment (Figure 1). All children had either one or more fractures prior to treatment and only two patients suffered fractures after commencing treatment. No major side effects were reported during the therapy. One child had spontaneous rupture of sclera and enucleation due to an accidental trauma while on therapy and he was referred to an ophthalmologist. One child died of pneumonia 2 months after the first cycle. Anaphylactic reaction was noticed in one child and no further pamidronate was given to him. Asymptomatic and mild hypocalcaemia was seen in some children.

The results we have seen in our patients are comparable with those reported in previous studies. A rapid rise in BMC and reduction of fracture incidence has been reported earlier [1–3]. At present, occurrence of a fracture or persistent bone pain are the only indications for pamidronate therapy in OI patients and asymptomatic OI patient without a previous fracture does not qualify for this therapy. Although the measurement of bone mass at the beginning of the treatment is desirable, it is not essential, as low bone mass alone is not considered an indication for this therapy.

Loss of bone mineral is a complication of OI and this further deteriorates the already impaired bone strength. Pamidronate is a potent inhibitor of osteoclasts and prevents bone resorption, leading to an increase in bone mass and restoring the bone strength to a certain extent. This may explain the reduction of fracture incidence seen after treatment with pamidronate. Long term suppression of bone resorption by prolonged pamidronate therapy, however, may interfere with the repair of microfractures, resulting in weakening of bone microarchitecture and increased incidence of fractures [4,5]. Hence pamidronate therapy should be stopped after 5–6 cycles. Adequate amounts of calcium and vitamin D3 should be given as adjuvant therapy and continued even after stopping pamidronate.

We also would like to emphasise the importance of prevention of falls in these children. Further, adequate nutrition and physical activities also should be ensured.

References

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To the Editors:

Use and interpretation of phrases in histopathology reports: interdisciplin ary meetings will help to reduce the confusion

The results of the research letter by Hewavisenthi and Fernando [1] have indicated that there is a wide variation in interpretation of phrases used in histopathology reports between pathologists and clinicians. Misinterpretation of histopathology reports could influence management of patients.

We wish to reiterate that this problem is avoided in other countries by discussion of patient management at interdisciplinary meetings, where pathologists are invariably present. In such situations, the final histopathology report becomes merely a summary, because most of the clinically relevant histopathological features have already been discussed at the meeting, with clarification of any queries [2]. Such meetings would also help to correlate clinical features, radiological findings and laboratory investigations with the ultimate pathology, and patient management, where histopathology is inconclusive. We feel that this is especially relevant in liver, renal and skin biopsies where despite the presence of histopathological changes, sometimes a definitive diagnosis cannot be made, but where therapeutic decisions could be arrived at after discussion.

Inter-disciplinary meetings should not be regarded as time consuming affairs, which would add to an already busy schedule. They are essential for optimal patient management. Furthermore, they are a forum for continuing medical education.

Reference


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