Editorial

Nutritional rickets: Some new insights

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Rickets is a generalized metabolic bone disorder, characterized by a failure of or delay in calcification of the cartilaginous growth plate in children whose epiphyses have not yet fused[1]. It results typically from an inadequate supply of calcium or phosphate to the zone of provisional calcification at the growth plate and to the mineralization front at the newly formed osteoid surface. Causes of rickets fall into 2 main categories, calciopenic and phosphopenic, based on the inability to maintain primarily serum calcium or serum phosphorus levels within the physiologic range[1].

Most natural foods contain little vitamin D and the quantities are generally insufficient to maintain vitamin D sufficiency. Thus, cutaneous synthesis of vitamin D_3 under the influence of ultraviolet radiation[2] is essential to maintain vitamin D sufficiency unless ingested foods are fortified or supplements provided. This is particularly true for the exclusively breastfed infant as breast milk contains very little vitamin D_3 or its metabolites. It has been estimated that breast milk from a vitamin D-replete mother contains 20-60 IU/L of vitamin D while the recommended intake for infants is 200 IU per day[4]. There is some evidence to suggest that if the lactating mother is adequately vitamin D supplemented (approximately 2000 IU per day), sufficient vitamin D and its metabolites are transferred in breast milk to maintain vitamin D sufficiency in the breastfed infant[5].

The newborn infant is protected from vitamin D deficiency for the first few months of life if born to a vitamin D-replete mother as 25(OH)D crosses the placenta readily and neonatal levels are approximately two thirds of maternal concentrations[6]. However, serum 25(OH)D concentrations in the breastfed infant fall to within the vitamin D deficiency range several months after birth, if no vitamin D supplements or sunlight exposure are provided[7]. Infants born to vitamin D-deficient mothers are not afforded this early protection and may present at or soon after birth with congenital rickets[8].

With the renewed worldwide emphasis on exclusive breastfeeding of infants for the first 6 months of life, infants in many developed countries are more at risk of developing vitamin D deficiency now than previously. The risk is heightened by the recommendations from the American Academy of Paediatrics that infants less than 6 months of age should be kept out of direct sunlight and that protective clothing and sunscreens should be used [9].

Besides exclusive breastfeeding, other factors influence the risk of the infant developing vitamin D deficiency. These include the zenith angle of the sun. Thus, those children living in countries of high latitude are more at risk than those living near the equator[10]. Additional factors include the degree of atmospheric pollution[11], the extent of skin coverage by clothing[12], the degree of skin pigmentation[13] and the time spent outdoors[14]. In the Middle East, social and religious norms (the practice of purdah and veiling) are primarily responsible for vitamin D deficiency in infants and their mothers[15].

Although vitamin D deficiency has generally been considered to be synonymous with nutritional or privational rickets, studies over the past 3 decades have highlighted the role of low dietary calcium intake in the pathogenesis of rickets in some communities. The peak prevalence of vitamin D deficiency rickets is characteristically between 6 and 18 months of age with a further smaller peak occurring during adolescence[16]. However, in several developing countries, such as Nigeria and Bangladesh[17,18], studies have highlighted the problem of calciopenic rickets and bone deformities (especially of the lower limbs) in children outside the infant and toddler age range. The affected children have dietary calcium intakes of approximately 200 mg per day with dairy products being almost absent from the diet. In these cases, calcium supplements alone (350-1000 mg per day) are effective in healing the disease and are more efficacious than vitamin D therapy alone[19]. In India, a randomized control trial of calcium or calcium and vitamin D for the treatment of young children and adolescents with rickets found that in the young children calcium supplements were as effective as calcium and vitamin

D in the treatment of the disease while in the adolescent group calcium alone was ineffective[20]. The authors concluded that calcium deficiency was likely to be the major factor in the pathogenesis of the disease in young children while vitamin D deficiency was the cause in the adolescents.

Nutritional rickets can no longer be regarded as being caused by vitamin D deficiency alone. The common pathway through which both dietary calcium deficiency and vitamin D deficiency act in the pathogenesis of rickets, is a reduction in intestinal calcium absorption below that which is required to meet the requirements of the growing skeleton[21]. Low dietary calcium intakes play a role in the pathogenesis of rickets through two mechanisms:

1. By being sufficiently low that however efficient the intestinal calcium absorption is, it is still too low to meet the bone requirements.

2. By increasing the catabolism of 25(OH)D and thus inducing vitamin D deficiency in children who have marginal vitamin D status.

Several countries have introduced public awareness and food fortification programmes and all infant formulae are fortified with vitamin D at a level of 400 IU/L. These measures have been effective in dramatically reducing prevalence of nutritional rickets in most developed countries. Despite these programmes however, the young breastfed infant remains at risk. Both United States and United Kingdom have recommended that all infants should receive vitamin D supplements to address this problem[9]. Further, recommendations for vitamin D supplementation during pregnancy and lactation have been made to prevent vitamin D deficiency in the pregnant mother and thus in her newborn infant.

The issue of low dietary calcium intake after weaning is a problem in many developing countries as calcium-rich foods such as dairy products are expensive and often inaccessible to most of the population. In developed countries, the variety of food choices and the current practice of fortifying some fruit juices with calcium make it easier for health professionals to advise mothers on correct food choices. In developing countries, the monotony and lack of food variety of the traditional diet makes it difficult for health professionals to provide cheap and effective methods to address the problem of low dietary calcium intake in young children.

Mainstay of treatment for infants and children with nutritional rickets is to correct vitamin D deficiency and ensure adequate calcium intake. Stanbury et al demonstrated that only small doses of vitamin D (450 IU per day) are required to achieve a rapid elevation in 1,25-$(OH)_2$D concentrations and more gradual return to normal of serum calcium and parathormone values[22]. Studies have shown, however, that more rapid healing is achieved with bigger doses of vitamin D (3000-15,000 IU per day) for 4-6 weeks. In children in whom compliance may be a problem, a single dose of 600,000 IU orally or intramuscularly has been shown to be effective with biochemical improvement occurring within a few days and radiographic evidence of healing appearing within 10-14 days[23]. A recent study has suggested that a single dose of 150,000 IU is equally effective as higher doses for treatment of active rickets and is not associated with the risk of hypercalcaemia that has been found with doses of 300,000 and 600,000 IU [24].

The breastfed infant with vitamin D deficiency generally does not require calcium supplementation unless symptoms of hypocalcaemia are present[25]. If the child with rickets has been weaned and is not receiving an adequate volume of milk as part of the diet, careful attention should be paid to ensure that dietary calcium intake approaches the recommended intake appropriate for the child's age. In developing countries this is of critical importance as several studies have suggested that dietary calcium deficiency is the major factor in the pathogenesis of the disease. Good results have been achieved with supplements ranging from 350-1,500 mg elemental calcium per day for a period of 6 months[19] and in such situations there appears to be little benefit from the addition of vitamin D to the therapy.

As far as nutritional rickets is concerned there certainly seems to be more to it than what meets the eye.

References

1. Pettifor JM. Rickets and vitamin D deficiency in children and adolescents. *Endocrinol Metab Clin N Am* 2005; **34**: 537-53.

2. Holick MF. Environmental factors that influence the cutaneous production of vitamin D. *Am J Clin Nutr* 1995; **61(Suppl 3)**:638S-45S.

3. Hollis BW, Roos BA, Draper HH. Vitamin D and its metabolites in human and bovine milk. *J Nutr* 1981; **111**: 1240-8.

4. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D and fluoride. Washington (DC): National Academy Press; 1997.

5. Ala-Houhala M, Koskinen T, Terho A. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 1986; **61**: 1159-63.

6. Hillman LS, Haddad JG. Human perinatal vitamin D metabolism 1:25 dihydroxyvitamin D in maternal cord blood. *J Pediatr* 1982; **84**:742-9.

7. Rothberg AD, Pettifor JM, Cohen DF. Maternal-infant vitamin D relationships during breastfeeding. *J Pediatr* 1982; **101**: 500-3.

8. Anatoliotaki M, Tsilimigaki A, Tsekoura T. Congenital rickets due to maternal vitamin D deficiency in a sunny island of Greece. *Acta Paediatr* 2003; **92(3)**: 389-91.

9. Gartner LM, Greer FR. Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake. *Pediatrics* 2003; **111(4 Pt 1)**: 908-10.

10. Pettifor JM, Moodley GP, Hough FS. The effect of season and latitude on in vitro vitamin D formation by sunlight in South Africa. *S Afr Med J* 1996; **86**: 1270-2.

11. Agarwal KS, Mughal MZ, Upadhyay P. The impact of atmospheric pollution on vitamin D status of infants and toddlers in Delhi, India. *Arch Dis Child* 2002; **87(2)**: 111-3.

12. Matsuoka LY, Wortsman J, Dannenberg MJ. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D_3. *J Clin Endocrinol Metab* 1992; **75**: 1099-103.

13. Holick MF, MacLaughlin JA, Doppelt SH. Regulation of cutaneous previtamin D_3 photosynthesis in man: skin pigmentation is not an essential regulator. *Science* 1981; **211**: 590-3.

14. Specker BL, Valanis B, Hertzberg V. Sunshine exposure and serum 25-hydroxyvitamin D concentrations in exclusively breastfed infants. *J Pediatr* 1985; **107**: 372-6.

15. Taha SA, Dost SM, Sedrani SH. 25-Hydroxyvitamin D and total calcium: extraordinarily low plasma concentrations in Saudi mothers and their neonates. *Pediatr Res* 1984; **18(8)**: 739-41.

16. Narchi H, El Jamil M, Kulaylat N. Symptomatic rickets in adolescence. *Arch Dis Child* 2001; **84(6)**: 501-3.

17. Oginni LM, Worsfold M, Oyelami OA. Etiology of rickets in Nigerian children. *J Pediatr* 1996; **128**: 692-4.

18. Fischer PR, Rahman A, Cimma JP. Nutritional rickets without vitamin D deficiency in Bangladesh. *J Trop Pediatr* 1999; **45(5)**: 291-3.

19. Oginni LM, Sharp CA, Badru OS. Radiological and biochemical resolution of nutritional rickets with calcium. *Arch Dis Child* 2003; **88(9)**: 812-7.

20. Balasubramaniam K, Rajeswari J, Gulab. Varying role of vitamin D deficiency in the etiology of rickets in young children vs. adolescents in northern India. *J Trop Pediatr* 2003; **49(4)**: 201-6.

21. Pettifor JM. Privational rickets: a modern perspective. *J R Soc Med* 1994; **87**: 723-5.

22. Stanbury SW, Taylor CM, Lumb GA. Formation of vitamin D metabolites following correction of human vitamin D deficiency: observations in patients with nutritional osteomalacia. *Miner Electrolyte Metab* 1981; **5**: 212-27.

23. Shah BR, Finberg L. Single-day therapy for nutritional vitamin D-deficiency rickets: a preferred method. *J Pediatr* 1994; **125**: 487-90.

24. Cesur Y, Caksen H, Gundem A. Comparison of low and high dose of vitamin D treatment in nutritional vitamin D deficiency rickets. *J Pediatr Endocrinol Metab* 2003; **16(8)**: 1105-9.

25. Ladhani S, Srinivasan L, Buchanan C. Presentation of vitamin D deficiency. *Arch Dis Child* 2004; **89(8)**: 781-4.

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