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7. Iron, Minerals and Trace Elements

METHODS

Literature Search

Timeframe: 1990–2004, in addition relevant earlier publications were considered.

Type of publications: randomised controlled studies; case-control or cohort studies; case reports; case series; expert opinion.

Key Words: calcium, chromium, copper, iodine, iron, manganese, magnesium, molybdenum, newborn, parenteral nutrition, phosphorus, selenium, trace elements, zinc.

Language: English.

IRON

Introduction

Iron is not routinely provided in parenteral nutrition mixtures and is often not a component of commercially available trace element preparations. Currently there are no well-defined recommendations regarding the optimum content of iron in parenteral feeds, and intravenous administration of iron remains problematic. One major concern is that of iron overload. Parenteral administration of iron bypasses the homeostatic control of gastrointestinal iron absorption, causing loss of protection from iron overload if excessive quantities are provided. An accumulation of excess iron has been reported in children receiving prolonged parenteral nutrition. In a study of 30 children aged 1–18 years receiving ferrous sulphate 100 μg/kg per day for an average period of 43 months, 12 children showed evidence of plasma and hepatic iron overload. Ferritin concentrations were >800 ng/ml in eight children (>1100 ng/ml in five) and correlated with duration of PN. The degree of iron deposition in either hepatocytes or Kupffer cells was most pronounced in children with the higher ferritin concentrations ((1) (LOE 2+)). Thus, iron status of children receiving long-term PN should be monitored by regular measurement of serum ferritin, and supplementation decreased if ferritin concentration is raised. Although Ben-Hariz et al suggested halving iron intake at ferritin concentrations of 500 ng/ml and stopping completely at 1000 ng/ml, these concentrations probably leave only a small margin of safety. There is, therefore, an argument for curtailing iron supplementation at lower plasma ferritin concentration.

A further concern over parenteral iron administration is that it may impair immune function and stimulate bacterial growth thus increasing the risk of infection by iron-requiring pathogens (2). Iron availability correlates with bacterial growth and virulence, facilitates viral replication and reverses the bactericidal effect of lactoferrin and lysozyme (3,4). Furthermore, the antibacterial effect of cytokines is mediated by intracellular iron depletion. Interferon, IL-1, and tumour necrosis factor enhance ferritin synthesis resulting in a shift of cellular iron into a storage compartment and downregulate transferrin receptor production decreasing cellular iron uptake and, thereby, iron availability for intracellular pathogens (5). Iron therapy has also been implicated in decreased phagocytosis and inhibition of CD4 and CD8 helper T cell proliferation while enhancing the function of suppressor T cells (6). Yet, several components of the immune response are depressed in iron deficiency. An impaired capacity for the generation of the oxidative burst has been observed in phagocytes from iron deficient children (7). McFarlane et al studied 40 children with kwashiorkor and low serum transferrin given nutritional support including iron supplements. Many of the children who received iron therapy died shortly after supplements were begun suggesting that provision of iron in a setting of low transferrin may have resulted in higher circulating free iron that could have contributed to the development of overwhelming infection and death (8). Septicaemia with Yersinia enterocolitica has been reported in healthy children overdosed with oral iron (9). Nevertheless, there is little clinical evidence that iron supplementation in parenterally fed children increases the risk of sepsis (10).

Adverse drug reactions associated with parenteral iron therapy are common, although side effects are mild and self limiting ((11,12) (LOE 2+)). In various series 2–5% of patients experience significant side effects. The processes leading to iron dextran induced symptoms are unclear, but include a type I (IgE-mediated) anaphylactic reaction which is caused by preformed dextran antibodies. Additional mechanisms include a type I anaphylactoid reaction that may be caused by transient overload of the transferrin molecule resulting in small amounts of free iron in the circulation (which appears to be dose related) and immune complex activation by specific IgG antibody. Symptoms include dyspnoea, wheezing, hypotension, nausea, vomiting, abdominal pain, arthralgia and myalgia. Most side-effects are mild and self-limiting with severe reactions occurring in a minority of patients and in conjunction with infusion of larger iron doses. An increased incidence of adverse effects has been reported in patients with collagen diseases. Despite previous

episodes of allergic reactions safe administration of iron dextran is possible following a pre-treatment protocol of methylprednisolone, diphenydramine and ephedrine. While total dose infusions of iron dextran may be associated with allergic manifestations the administration of the standard maintenance doses (estimated at 1–2 mg/day up to 10–15 mg/day) may be well tolerated (11,13).

There is a paucity of studies on the effects and complications of intravenous iron in children. No adverse effects were reported in 14 children who received 15 mg/kg of iron dextran during a two hour period (13), in 2 children who received IV iron at a dose of 250–500 mg at an infusion rate of a 100 mg/min (14), or in 5 premature infants given iron dextran at a dose of 10–450 μg/kg per day (15). Similarly, no complications were observed in a study of 14 very low birth weight infants receiving IV iron supplementation at a dose of 200–250 μg/kg per day ((16) (LOE 1+)).

The ability of iron both as Fe^{3+} (bound form) or Fe^{2+} (free iron) to generate free oxygen radicals has also raised concerns regarding safety. In addition, parenteral lipid emulsion also generates peroxides (17). The rich content of double bonds of the lipid emulsion makes it a good substrate for iron-induced peroxidation. Light induced generation of peroxides in PN solutions and the interaction of iron complexes (iron dextran) with photons or substrates of photo-oxidation, such as vitamins or polysorbate, could explain the unexpected observation that bound iron is protective against spontaneous peroxide generation in PN solutions (18).

The compatibility of iron with PN solutions has not been clearly established. Iron dextran cannot be added to lipid emulsions or all-in-one mixes as it results in destabilisation of the emulsion. Compatibility of iron dextran has been shown in amino acid-glucose solutions for up to 18 hours (19). Ferrous citrate is also compatible with PN solutions, with no observed precipitation during infusion periods of 18–24 hours (20).

Whether or not there is a need for routine iron supplementation of PN remains controversial. A special concern is the low birth weight infant because of possible increased risk of infection observed following intramuscular iron (21). Arguments in favour of iron supplementation in VLBW infants include their low iron stores, rapid growth rate, increased requirements for iron when erythropoesis resumes at approximately 2 months of age, and caution required in relation to repeated blood transfusion. It has been estimated that these newborns need 700 to 1000 μg/kg per day to reach iron balance (15,16) although considerably lower doses may suffice ((22) (LOE 4)); possibly erythropoeitin is needed to use the iron administered. In term infants receiving PN it is estimated that the daily parenteral iron requirement is 100 μg/kg per day (22). Although iron reserves should be adequate to supply red cell production for 3–5 months, iron deficiency has been shown to develop much sooner. How early parenteral iron supplements should be commenced in infants and children receiving PN will depend on the underlying pathology and degree of blood loss. In short term PN of a few weeks no adverse effects resulting from lack of iron supplementation have been observed (10). During long-term PN the child's iron status should be monitored closely and supplementation begun as soon as impending deficiency is identified.

In summary, iron supplementation with iron dextran added to amino acid-glucose solutions can be safely administered at maintenance doses. Preterm infants require parenteral iron but may also require erythropoietin for utilisation. Term infants and older children probably do not need iron supplementation when receiving short-term PN. Timing the initiation of iron supplementation in the diverse population of children requiring PN should be based on their underlying morbidity, previous surgical interventions and potential blood losses. In children receiving parenteral iron supplementation close monitoring of iron status is mandatory to avoid iron overload.

Recommendations

- Patients receiving long-term PN (>3 weeks) should receive iron supplementation. **GOR C**
- In children who receive long-term iron supplementation in PN, the risk of iron overload requires regular monitoring of iron status using serum ferritin. **GOR B**
- Iron supplementation should be provided to very low birth weight infants receiving PN. **GOR B**
- The dose of iron for infants and children of 50–100 μg/kg per day is based on calculations extrapolated from studies showing that lower doses may not be sufficient to maintain iron balance and represents ''expert opinion''. The dose in premature infants may need to be 200 μg/kg per day. During short term PN (i.e. <3 weeks) iron supplementation is usually unnecessary. **GOR D**
- The preferred modality of iron administration is as regular daily doses. The ideal formulation (dextran, citrate etc) has not been adequately delineated but data in adults regarding iron dextran shows it to be safe and efficacious. **GOR D**

TRACE ELEMENTS

Introduction

Chromium, copper, iodine, manganese, molybdenum, selenium and zinc are essential micronutrients involved in many metabolic processes. Parenteral nutrition aims to meet nutritional needs while avoiding complications; precise requirements for individual nutrients remain a matter of debate ((23) (LOE 2+)). Trace elements are involved in enzymatic activities and immunologic

reactions. Although toxicity is infrequent, it is well described in patients receiving PN ((24) (LOE 2+)). Low-birth-weight infants (LBW) are at risk of trace element deficiency both because they are born before adequate stores can be acquired and because of the demands of their rapid growth ((25) (LOE 2++); (26)). Parenteral mineral and trace element delivery are calculated to prevent the development of deficiency syndromes ((27) (LOE 2+)) and to match in-utero accretion rates ((28) (LOE 2+)). Parenteral solutions are contaminated with metals such as aluminium and chromium; these require monitoring during long-term PN ((29)(LOE 2+)). A change from glass to plastic packaging for PN products may have implications for trace element supplementation through decreased contamination. Trace element status should be closely monitored in cholestatic patients and trace element preparations may need to be discontinued to avoid copper toxicity. Patients with renal impairment may not be able to excrete selenium, molybdenum, zinc and chromium ((29,22) (LOE 1+)). When taking blood samples for trace element analysis it is important to avoid contamination of the specimen.

Recommendations

- Trace elements should be supplied with long-term parenteral nutrition. **GOR D**
- Trace elements should be periodically monitored in patients on long-term parenteral nutrition. **GOR D**

Chromium

Chromium (Cr) is an essential micronutrient required for carbohydrate and lipid metabolism. Cr deficiency has been described in patients receiving long-term PN, but patients receiving PN also have been reported to show increased serum Cr level ((30) (LOE 2+)). Efforts are required to find PN components with low or, if possible, no Cr contamination (30). High serum Cr competes with iron for binding to transferrin and, hence negatively interferes with iron metabolism and storage ((31) (LOE 3)). A daily intake of 0.2 μg/kg per day has been recommended for infants and children (maximum of 5 μg/day) receiving PN ((22) (LOE 2++)), although there is some evidence that lower intakes would be adequate ((32) (LOE 2+)). Supplementation is unnecessary since Cr contaminates PN solutions to a degree that satisfies requirements ((33) (LOE 2+)).

Recommendation

- Cr contaminates PN solutions to a degree that satisfies requirements, therefore, additional supplementation of Cr is considered unnecessary. **GOR C**

Copper

Copper (Cu) is a component of several enzymes, including cytochrome oxidase, superoxide dismutase (Cu/Zn SOD), monoamine oxidase and lysyl oxidase. Copper concentrations in plasma and cells as well as copper metalloenzymes are indicative of copper status ((34,35) (LOE 2++)). Monitoring plasma concentration of both Cu and caeruloplasmin, the major Cu transport protein, should be considered during PN ((36) (LOE 2+)). However, superoxide dismutase (SOD) activity in erythrocytes seems to be a more sensitive indicator of Cu deficiency than plasma concentration of Cu or caeruloplasmin ((37) (LOE 2++)). Other indicators of Cu status include neutrophil counts (low in deficiency), SOD activity, platelet cytochrome-c oxidase activity and platelet copper concentration ((35) (LOE 2++)). Cu should be carefully monitored in patients with cholestatic liver disease ((22,38) (LOE 2++)).

Plasma total Cu and caeruloplasmin are invariably reduced in children with burns ((36) (LOE 2+)). PN in these patients must be supplemented with more than 20 μg/kg Cu to avoid deficiency ((39) (LOE 2+)). The high Cu content in gastrointestinal fluid means that losses should be balanced by a higher Cu intake (increased by 10 – 15 μg/kg) in PN (22). A routine intravenous supply of 20 μg/kg per day copper for infants (preterm and term) and children is recommended ((22) (LOE 2++)).

Recommendations

- Parenterally fed infants and children should receive an intravenous supply of 20 μg/kg per day copper. **GOR D**
- Plasma copper and caeruloplasmin concentrations should be monitored in patients receiving long term PN and in parenterally fed patients with burns or with cholestasis, and adjustment of copper supply be considered accordingly. **GOR D**

Iodine

Iodine is an essential part of the thyroid hormones, thyroxin (T4) and tri-iodothyronine (T3), which are necessary for cellular metabolism and maintenance of metabolic rate. Thyroid function remained normal and serum iodine levels were not reduced in children receiving long-term PN without iodide supplementation, probably due to iodine contamination of the solutions and skin absorption of topical iodinated disinfectant ((40) (LOE 2+)). It is also possible in these patients that there was some absorption of iodine present in the ingested food. However, a daily dosage of 1 μg/d is recommended for infants and children receiving PN ((22) (LOE 2++)). Now

that use of iodine for skin cleaning is relatively uncommon, there may need to be a reassessment of iodine requirements.

Recommendation

- Parenterally fed infants and children should receive a daily iodine supply of 1 μg/d. **GOR D**

Manganese

Manganese (Mn) is a component of several enzymes including mitochondrial superoxide dismutase and also activates other enzymes such as hydrolases, kinases and transferases. High Mn intake during PN is probably one of several factors contributing to the pathogenesis of PN associated cholestasis or other hepatic dysfunction ((41) (LOE 3); (38) (LOE 2++); (42) (LOE 2++); (43) (LOE 1)). Mn should, therefore, be carefully administered, particularly in patients receiving long-term PN ((38) (LOE 2++); (44) (LOE 3); (45) (LOE 2+)). Studies using magnetic resonance images (MRI) have reported high-intensity areas in basal ganglia, thalamus, brainstem and cerebellum due to Mn intoxication with disappearance of symptoms and MRI abnormalities after withdrawal of manganese administration ((46) (LOE 2+); (47) (LOE 3); (48) (LOE 3); (44) (LOE 3)). As central nervous system deposition of Mn can occur without symptoms, regular monitoring of manganese blood concentration should be performed in children on long-term PN. Taking into account the hazards of high Mn levels in children receiving long-term PN, a low dose regimen of no more than 1.0 μg (0.018 μmol)/kg per day (maximum of 50 μg/d for children) is recommended ((22,38) (LOE 2++)) together with regular examination of the nervous system (38).

Recommendation

- In children receiving long-term PN, a low dose supply of no more than 1.0 μg (0.018 μmol)/kg per day (maximum of 50 μg/d for children) is recommended. **GOR D**

Molybdenum

Molybdenum (Mo) is essential for several enzymes involved in the metabolism of DNA. To our knowledge there are no reports of Mo deficiency in infants. However, low-birth-weight infants (LBW) might be at particular risk for Mo deficiency ((49) (LOE 2+)). Excess of Mo interferes with Cu metabolism. According to some authors an intravenous intake of 1 μg/kg per day (0.01 μmol/kg per day) seems to be adequate for the LBW infant ((49) (LOE 2+)). 0.25 μg/kg per day is recommended for infants and children (to a maximum of 5.0 μg/day) ((22) (LOE 2++)). Intravenous Mo supplements are recommended only with long-term PN.

Recommendations

- An intravenous molybdenum supply of 1 μg/kg per day (0.01 μmol/kg per day) seems adequate and is recommended for the LBW infant. **GOR D**
- For infants and children an intravenous molybdenum supply of 0.25 μg/kg per day (up to a maximum of 5.0 μg/day) is recommended. **GOR D**

Selenium

Selenium (Se) acts as an antioxidant by being an essential component of active glutathione peroxidase (GSHPx), an enzyme that may protect against oxidative tissue damage. Oxidative injury, particularly in the first days of life, is associated with long-term complications of prematurity ((50) (LOE 2++)). Low Se status has been documented in pre-term infants and has been implicated in oxidative diseases such as bronchopulmonary dysplasia and retinopathy of prematurity ((51) (LOE 3); (50) (LOE 2++)). Tissue concentrations of Se and activities of selenium-dependent glutathione peroxidase (Se-GSHPx) are useful indicators of Se status ((52) (LOE 2+)). In order to identify Se deficiency in children receiving PN, it has been recommended that plasma and red cell selenium concentration and Se-GSHPx are monitored ((53) (LOE 3)). Erythrocyte and platelet GSHPx activity are sensitive indexes of Se status in PN patients ((54) (LOE 2+); (55) (LOE 2++)).

Several authors have cautioned against high doses of selenium supplementation because of the risk of toxicity. However there have been no reports of selenium toxicity in infants. Se is also known to be important in thyroid metabolism but selenium deficiency does not seem to play a major role in neonatal hypothyroidism ((56) (LOE 2++)). A non-specific myopathy has also been associated with Se deficiency on long-term home PN ((57) (LOE 3)). A dose of 2–3 μg/kg per day has been recommended for LBW infants, although the optimal form and dose remain unclear ((22) (LOE 2++); (58) (LOE 2++); (56) (LOE 2++)). It should be kept in mind that Se supplementation may also affect copper metabolism ((59) (LOE 1)).

Se content in mature breast milk ranges from 6–28 μg/L in the USA and Europe (52) representing an average intake of around 2.5 μg/kg per day with perhaps an 80% absorption. Serum Se concentration is lower in

PN fed infants than those who are enterally fed with either formula or mother's milk using current recommended intakes ((60) (LOE 2++)). Premature infants (particularly the very low birth weight) might require double the currently recommended Se intake of 1–3 μg/kg per day. Selenite is retained better than selenate, although it has a more variable absorption. The organic compound selenomethionine is chemically stable and well retained by the body and can be used in parenteral nutrition.

Recommendation

- An intravenous selenium supply of 2 to 3 μg/kg per day is recommended for parenterally fed LBW infants. **GOR D**

Zinc

Zinc (Zn) is involved in the metabolism of energy, proteins, carbohydrates, lipids and nucleic acids and is an essential element for tissue accretion. Urinary Zn excretion occurs in the parenterally fed infant. Some amino-acids like histidine, threonine, and lysine have been shown to bind Zn increasing its renal ultrafilterability ((61) (LOE 2+)). Increased urinary losses of Zn and decreased plasma concentrations occur following thermal injury in children ((39) (LOE 2+)). Premature infants need a higher zinc intake than term infants because of their rapid growth: 450–500 μg/kg per day to match in-utero accretion rate ((62) (LOE 2+)). Standard trace element preparations do not supply this amount, and additional zinc (zinc sulphate) may need to be added to PN fluid in the preterm infant, or those patients with high zinc losses e.g. from diarrhoea, stomal losses or severe skin disease ((63) (LOE 2+)). Recommendations are for an intravenous intake of 250 μg/kg per day and 100 μg/kg per day respectively for infants less or more than 3 months of age, and 50 μg/kg per day for children (maximum of 5.0 mg/day) ((22) (LOE 2++)). Zn is the only trace element that should be added to solutions of patients on short-term PN (22).

Recommendations

- Parenteral zinc supply is recommended in daily dosages of 450–500 μg/kg per day for premature infants, 250 μg/kg per day for infants less than 3 months, 100 μg/kg per day for infants aged 3 months or older, and 50 μg/kg per day (up to a maximum of 5.0 mg/day) for children. **GOR D**
- Excessive cutaneous or digestive losses of zinc require additional supplementation. **GOR D**

CALCIUM, PHOSPHORUS AND MAGNESIUM

Introduction

The requirements of calcium (Ca) and phosphorus (P) are considered together because the majority of both elements are found together as components of the bone mineral apatite [$Ca_5(PO_4)_3OH$]. 97% of whole body Ca is stored in apatite together with 80% of whole body P (64,65). The molar Ca: P ratio is 1.3 in the whole body and 1.67 in apatite. Serum calcium exists in three fractions: ionised calcium (approximately 50%), protein-bound calcium (approximately 40%), and a small amount of calcium that is complexed, primarily to citrate and phosphate ions. Serum calcium is maintained at a constant level by the actions of several hormones, most notably parathyroid hormone and calcitonin. Calcium absorption is by the passive vitamin D-independent route or by the active vitamin D-dependent route.

Calcium

Calcium is the most abundant mineral in the body. Approximately 99% of total body calcium is found in the skeleton, with only small amounts in the plasma and extra-vascular fluid. Precise calcium requirements are uncertain. In the newborn infant the total body Ca content is around 28 g with 98% in bone. Based on body composition measurements, approximately 1kg of calcium is deposited in the skeleton between birth and adulthood. Daily accretion rates for boys and girls must average around 150 and 200 mg calcium/d, however, since growth is not uniform, accretion rates may be as high as 400 mg calcium/d during infancy and puberty. A recent study using dual energy x-ray absorptiometry found an average bone calcium accretion rate of 220 mg/d and 317 mg/d in girls and boys respectively during stage III puberty (66). The amount of dietary calcium needed to satisfy the demand for skeletal growth and mineralization is greater than the theoretical accretion rate because of incomplete calcium absorption and losses from skin, urine and gastrointestinal tract. The limited information available regarding calcium needs in children is reflected in wide variation in recommended intakes (22,67,68), and is generally based on recommended oral intake of calcium. Administration of intravenous calcium during parenteral nutrition is limited by solubility.

Phosphorus

Phosphorus (P) is a major intracellular mineral and also crucial for bone mineralisation. In newborn infants total body phosphorus is around 16 g (rising to 600–900 g in an adult) with 80% in bone and 9% in skeletal muscle. In the kidney 85–90% of the filtered phosphate is reabsorbed. In the presence of a low phosphate intake the kidney retains phosphate and it disappears from the

urine. Hypercalcaemia and hypercalciuria may result from phosphate deficiency. Excess phosphate intake may lead to hyperphosphataemia, hypocalcaemia and secondary hyperparathyroidism. Deficiency of phosphate results in bone demineralisation and rickets. Extreme hypophosphataemia can be precipitated by nutritional restitution ('refeeding syndrome') and can result in muscle paralysis, cardiac dysfunction and respiratory failure.

Magnesium

Magnesium is the fourth most abundant metal in the body and the second most abundant intracellular electrolyte. In the newborn infant the total body Mg is around 0.8 g (rising to 25 g in an adult) with 60% in bone. The physiological importance of magnesium lies in its role in skeletal development and in the maintenance of electrical potential in nerves and muscle membranes. Calcium homoeostasis is controlled in part by a Mg requiring mechanism which releases parathyroid hormone. Plasma Mg represents only 0.3 to 11% of total body stores and total plasma Mg concentration does not estimate the biologically active fraction-ionised Mg (69). Inadequate intakes of Mg, Ca and P may induce rickets, fractures, impaired bone mineralization and reduced linear growth (70,71).

Parenteral Supply of Ca and P

In selecting compounds suitable for parenteral nutrition it must be considered that Ca cations may precipitate with inorganic phosphate anions. To some degree this can be avoided by mixing Ca and phosphate with amino-acids and glucose (72–75) but even more so by using organic phosphorus compounds (76–85). Glycerophosphate is available as di-sodium salt in Europe. Parenteral solutions containing Ca may cause damage to peripheral veins, and extravasation may induce severe tissue necrosis. The adequacy of Ca and P intakes in young infants should be adjusted until both are excreted simultaneously with low urine concentrations (1–2 mmol/L) indicative of a slight surplus (86).

Calcium, Phosphate and Magnesium in Children

Taking into account percentage absorption from the diet, parenteral intakes of Ca, P and Mg can be estimated from Recommended Nutrient Intakes (RNI), the amount of nutrient that is enough, or more than enough, for about 97% of people in the group (87). Around 66% of calcium is absorbed from breast milk, but net dietary absorption in older children is around half this level. Absorption of phosphorus is about 60% with the RNI for phosphorus being set equal to that for calcium in mmol (87). Between 20-50% of dietary magnesium is absorbed, but much more can be absorbed when dietary intakes are low. Recommendations for parenteral intake of Ca, P and Mg are given in the tables below. Blood concentrations require periodic monitoring; phosphate concentration may drop suddenly in malnourished patients starting PN.

TABLE 7.1. *Recommended parenteral Ca, P, and Mg intake*

Age	Suggested parenteral intake Ca mg (mmol)/kg	Suggested parenteral intake P mg (mmol)/kg	Parenteral intake Mg mg (mmol)/kg
0–6 m	32 (0.8)	14 (0.5)	5 (0.2)
7–12 m	20 (0.5)	15 (0.5)	4.2 (0.2)
1–13 y	11 (0.2)	6 (0.2)	2.4 (0.1)
14–18 y	7 (0.2)	6 (0.2)	2.4 (0.1)

Recommended parenteral calcium, phosphorus and magnesium intakes for infants and children are shown in Table 7.1. **GOR D**

Calcium and Phosphorus in the Premature Newborn

The total amounts of Ca and P accreted in foetal life are strongly correlated with body weight (88–91). This was confirmed for the bone mineral content in newborn infants including those with intrauterine growth retardation (92). In preterm infants the retention of Ca and P is proportional to growth (93). Foetal bone mineral accretion rate can be achieved in preterm infants given sufficient supplementation with Ca and P (86).

Requirements

The foetal mineral accretion rate corresponds to 2.0 mmol Ca/10 g newly grown body weight and 1.52 mmol P respectively. This has been proposed as a reference mark for parenteral nutrition of infants born preterm and at term. The dosage should be adjusted to the individual growth per body weight. Preterm infants growing at a rate of 20 g/d need 4.0 mmol Ca and 3.0 P per infant and day to meet the foetal requirements. If the baby weighs 1.0 kg this dose would correspond to 4 and 3 mmol/kg per day. If the baby weighs 2 kg then this dose would correspond to 2 and 1.5 mmol/kg per day. If the baby is growing at a slower rate (10 g per day) the dose would correspond to only 1 mmol Ca and 0.75 mmol P/kg per day. Therefore, a wide range covers the spectrum of requirements: Ca 1.0–4.0 mmol/kg per day, P 0.75–3.0 mmol/kg per day which provides a molar Ca:P ratio of 1.3. (64,65).

Recommendations

- Growing newborn infants should usually receive 1.3–3 mmol calcium/kg per day and 1–2.3 mmol phosphorus/kg per day, with a Ca:P ratio (mol/mol) in the range of 1.3–1.7. **GOR D**

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