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A brief Review: Mineral Isotopes

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ABSTRACT
An adequate mineral intake part of a healthy diet for child and women which supports appropriate growth and development and provides protection against children. It helps to prevent anaemia and future diseases for example osteoporosis, children have hampered the accurate assessment of their mineral utilization. Enriched isotopes use as tracers haven proven to be valuable in studies of the absorption and metabolism of minerals, they can be used in high-risk population groups such as infants, children, and pregnant or lactating women. The mineral bioavailability in humans and animals can be obtained by using isotopic tracers. It has a number of advantages in human nutrition studies which include radioisotopes, stable isotopes, mass balance measurements, and analytic method. There is no exposure to radiation with stable isotopes, and some minerals have no radioisotope that can be used as a tracer. Study conducted on using isotopes of Zn, Ca, Fe, and Mg. Although stable isotopes have been more extensively used in humans.
Key words: *Minerals, mass imbalance, stable isotopes, zinc absorption, calcium absorption.*

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I. Introduction

Mineral isotopes: Mineral isotopes are required for the field of nutritional studies which are used for studying the flow of nutrients through the human body. Since they are safe and non-radio-active they can be used in infants and pregnant women. stable isotope fractionations between minerals are functions of the fundamental vibrational frequencies of the minerals.

Mineral nutrition not only meets children's growth and developmental needs, but also may limit or prevent disease processes (e.g., diarrhoea) and protect against future diseases (e.g., adult osteoporosis). Children are a particularly challenging group in which to perform nutritional research, not only because of their rapid growth, but also because of the difficulties inherent in dietary regulation and sample collection in children. Use of stable isotopes offers a unique opportunity to meet the need for evidence-based dietary guidelines. Stable-isotope studies may also provide physiologic information regarding nutrient metabolism that is otherwise unobtainable in children. There are numerous methods for evaluating mineral requirements in children. One important approach to assessing requirements is to determine the amount of minerals absorbed and retained by children consuming diets providing various intakes. This can be done by several methods. These include mass-balance measurements, radioactive mineral administration, and stable-isotope methods. Isotopes are elements with identical chemical and functional properties but different in atomic mass due to having different number of neutrons in the nucleus. The difference in mass makes it possible for the isotopes to be analytically set apart from each other metabolic fate of each isotope can be traced when introduced into a biological system. Stable isotopes refer to non-radioactive isotopes occurring naturally, but elements or compounds can be synthesised that are enriched compared with the naturally occurring amount. **(Abrams SA *et.al*.., 1993)**

In nutrition, stable isotopes can be used to measure the amount of water or other nutrients in the body or the amount of an ingested nutrient that is absorbed and metabolised or excreted. They can be applied to determine the rate of absorption, utilisation or synthesis of proteins, fats or carbohydrates. Stable isotope techniques are non-invasive, and do not involve any radiation hazard. In nutritional assessments, stable isotope labelled compounds are given orally, often as part of a test meal, or intravenously and after a period of time urine, saliva, blood or breath samples are collected and the enrichment of the administered isotope in the compound of interest is measured using MS or infrared spectroscopy techniques. **(V.O. Owino *et.al*., 2015)**

Mass balance measurements

In these studies, the net dietary balance, often referred to as retention, of the nutrient is determined from simultaneous measurements of intake and excretion (urinary and fecal) of the nutrient. The effects of different intakes on balance are calculated and an attempt is made to determine an optimal intake on the basis of these data. Mass-balance studies, however, have many limitations, especially when applied to paediatric populations. These include potential errors in identifying accurately both intake and total excretion of minerals and the high cost and substantial difficulty of conducting long-term nutrition balance studies. An additional problem is that mass-balance studies do not provide direct information regarding key aspects of mineral metabolism. For example, endogenously secreted (and then excreted) mineral cannot be distinguished from non-absorbed dietary intake. Furthermore, information regarding the kinetics of mineral transport and utilization is not provided by mass-balance studies. Finally, it is very difficult to evaluate nutrient-nutrient interactions (e.g., calcium-iron interactions) when using mass-balance studies. Stable isotopes are now known to exist in numerous elements with the key feature being that there are differing numbers of neutrons in the elements' nucleus. Thus, one element can share the same atomic number, but differing mass numbers, which identifies the isotope. These differences do not alter to any great extent the chemical properties of the atom, but of course, do change the physical properties. They have long been a safe tool for assessing various aspects of human nutrition, and continue to be so, often in potentially vulnerable groups including, for example, premature infants, children in both health and Disease.

Radio-active Isotope

Radioactive isotopes began to be widely used during the 1940s to study mineral absorption and turnover. Iron and calcium radioisotopes continue to be used in studies of both healthy adults and those with mineral-deficiency conditions. However, concern exists regarding the appropriateness of using radioactive isotopes in research involving children or pregnant women. It is likely that the increasing availability of both stable isotopes and resources for their analysis will increase this trend toward investigators using stable rather than radioactive isotopes in mineral studies involving adults as well as children. Stable isotopes have been used as tracers in human nutritional studies for many years. A number of isotopes have been used frequently to assess body composition, energy expenditure, protein turnover and metabolic studies in general, such as deuterium 2 Hydrogen, 18 Oxygen, 13 Carbon and 15 Nitrogen. **(Jackman LA *et.al.*., 1997)**

Goals of mineral stable-isotope studies in children

Stable-isotope techniques can facilitate research into the mineral requirements of children in several ways, as follows:

- relating mineral metabolism to growth and pubertal development
- evaluating dietary mineral interactions
- evaluating the effects of acute and chronic illnesses on mineral absorption and metabolism, and
- evaluating the mineral needs of breast- and formula fed infants to consider the optimal intake of minerals in formulas or other foods for infants.

Evaluating dietary mineral interactions

Vitamin and mineral supplements are being taken by an increasing number of children and women. The interactions of the minerals within these supplements, or between supplemental and dietary minerals, have not been well studied in adults or children. For example, combining calcium and iron supplements may decrease iron absorption from the supplements. Multimineral stable-isotope studies can be used to directly assess the consequences of multimineral supplementation on mineral bioavailability.

Evaluating effects of mineral absorption and metabolism:-

This lack of data is the basis of uncertainty regarding the need for, and potential risks and benefits of, mineral supplementation. For example, we showed that high calcium intakes did not prevent a net calcium loss (i.e., a negative calcium balance) in adolescent girls with anorexia nervosa. Relatively few other paediatric conditions have been similarly evaluated.

Other minerals are being increasingly linked to diseases states in children. For example, zinc deficiency may be an important contributor to morbidity from diarrheal illnesses. Stable isotopes may be used to evaluate the magnitude of direct secretory zinc losses in diarrhoea or chronic malabsorptive conditions as well as the effect of supplementation on these losses and body pools of zinc. These assessments can now be done safely and readily using non-radioactive, stable isotopes which are available for calcium, zinc, magnesium, and iron. Mineral absorption can be assessed without collecting fecal samples. Kinetics are assessed with blood and urine collections, usually over 5-10 days**. (Smith SM, *et.al.*., 1999)**

Isotopic analysis methods

Isotope method belong to the most modern and up-and-coming analytical methods. They are used for determination of origin and composition of products. The equipment in CTL is as follows: nuclear magnetic resonance spectrometer (NMR) and isotope ratio mass spectrometer (IRMS). Laboratory unit of isotopic analyses is equipped with large number of accessories for the sample preparation and for control of process Isotopic methods (SNIF-NMR, IRMS, ICP-MS) determine ratio of stable isotopes of basic elements of organic matter. SNIF-NMR method determines D/H ratio in various sites of organic molecules e.g., ethanol. IRMS method determines D/H, 13C/12C, 18O/16O ratios in products and in their components. ICP-MS method determines isotope ratio of nearly any element. After determination of isotope ratios followed by their comparison with standards one is able to indicate.

Isotopic methods are indispensable in determination of origin of the goods produced from natural sources. Especially in the field of alcohol and alcoholic beverages they have the primary importance for disclosure backdoor moving of the goods and for detection of adulteration of the goods. The possibilities of isotopic methods and quality of the interpretation of measured results depend on the range of the databases of isotopic parameters of the products and their components.

Analytic methods

Isotope can be isolated from most serum and urine samples by precipitation with ammonium oxalate. Adequate amounts of calcium can usually be recovered from 3 mL urine or 0.5 mL serum. Fecal samples require acid digestion and sometimes ion exchange chemistry before precipitation and analysis. After precipitation, samples are baked in a muffle furnace and resuspended in dilute nitric acid. Five microliters of suspension are loaded onto a multisampling turret and placed in the mass spectrometer for analysis. With TIMS, calcium samples are analysed indirectly by using a dual-filament technique. For magnetic sector instruments, accuracy of this technique for natural-abundance samples is 0.1–0.2% of accepted values. Precision, including sequential measurement of the same sample (on different filaments) over a period of time, is similar.

Compartmental modelling

The compartmental model used for kinetic interpretation is similar to that originally described in adults. This model is based on a series of sequential pools before calcium deposition in the "deep" bone calcium pool. Bone calcium deposition (V_o+) is the flow rate of calcium to the final pool. The compartmental modelling of the data is done with the aid of the SAAM program or its SAAM II successor. **(Neer *et al.*, 1997)**

Some significant minerals used as isotopes in clinical trials

The methods and results of specific mineral research studies involving stable isotopes. The two primary minerals that will be described are calcium and iron, followed by briefer discussions of magnesium and zinc.

Calcium: -

Calcium stable isotopes

There are 6 naturally occurring stable isotopes of calcium. Typical doses of isotopes used in clinical studies. The most abundant calcium isotope, 40Ca (96.97% natural abundance), is rarely used in nutrition research, although very highly enriched (>99.9%) 40Ca can be administered over time to wash out the lower-abundance isotopes. The large quantity of 40Ca needed for this purpose makes this relatively impractical. The existence of a very-low-natural-abundance isotope, 46Ca (0.003% natural abundance), and 4 other low-abundance isotopes makes calcium a favourable mineral for tracer studies. Calcium stable isotopes are usually purchased as powdered calcium carbonate. Preparations for human use are made under sterile conditions. The powder is dissolved in nitric oxide and then, after drying, is converted to calcium chloride by mixing it with sodium chloride. Isotopes are then filtered and tested for sterility and pyrogenicity before use in humans.

Iron:-

Although iron stable-isotope use was reported in the 1960s, as with calcium, there were relatively few studies that used these isotopes until the early 1980s, when they began to be used primarily in studies involving adults. To date, most paediatric studies using iron stable isotopes have been conducted in preterm or full-term infants. This inclusion of full-term infants in iron stable-isotope studies contrasts with the virtual lack of such studies for calcium. This difference is presumably because of the relatively greater clinical problem of iron deficiency compared with calcium deficiency for otherwise healthy full-term infants and toddlers.

Iron stable isotopes

There are 4 naturally occurring iron stable isotopes of these, the lowest-abundance isotopes, 58Fe and 57Fe, are most commonly used in human nutrition research. Iron stable isotopes are usually provided as iron metal and are converted to ferrous sulphate before oral administration. Both the supply and cost of these isotopes have remained relatively constant or have decreased in recent years. Because dosing of iron stable isotopes is dependent on enriching the circulating body iron pool, the dose administered is usually dependent on the subject's weight, and increases in proportion to weight and haemoglobin concentration.

We use [58Fe] citrate as the form of iron to be administered when it is given intravenously. There may be a very small risk of an allergic reaction associated with the use of intravenously administered iron. An adverse reaction is extremely unlikely because of the form and the small doses (always <0.5 mg total Fe) used. However, because of this potential risk, we have chosen to administer iron isotopes intravenously only within a hospital setting. We administer the [58Fe] citrate over 30 min with careful monitoring of vital signs. **(Matkovic V, *et.al.*, 1990)**

$$^{57}Fe_{inc} = \frac{[57Fe/^{56}Fe_{enr} - {}^{57}Fe/^{56}Fe_{base}] \times Fe_{circ} \times NA_{57}}{^{57}Fe/^{56}Fe_{base}}$$

Magnesium: -

The measurement of magnesium absorption, endogenous excretion, and kinetics with stable isotopes in children is a significant methodologic challenge. The difficulty lies in the fact that, unlike calcium, zinc, and iron, which have ≥4 naturally occurring stable isotopes, there are only 3 stable isotopes of magnesium. None of the 3 isotopes of magnesium are of low abundance (i.e., <5%). Therefore, to achieve measurable enrichment of a serum or urine specimen, a relatively large dose of isotope needs to be given. This dose represents a significant fraction of the exchangeable magnesium pool and therefore may not function as a true tracer. Furthermore, although magnesium isotopes are readily available for purchase, the large doses required make these studies somewhat expensive to perform. We recently completed a study measuring magnesium absorption and kinetics in boys and girls aged 9–14 y. We showed a close correlation between weight and fat-free mass and both the size of the exchangeable pool of magnesium and the rate at which this pool exchanges with the longer-term storage pool. These relations are closer for magnesium than for calcium. These relations provide support for basing dietary magnesium requirements in children on body-composition measures such as body weight or, when available, fat-free mass. These studies have further suggested that current intakes of magnesium may only be marginally adequate during the rapid growth of early adolescence.

Zinc: -

There has been increased interest in zinc in paediatrics because of recent studies suggesting an association between low zinc status and infections, especially diarrheal illnesses and respiratory infections. The possibility of using supplemental zinc to decrease the consequences of these infections or to enhance growth in children, especially in underdeveloped nations, is an important area for ongoing research.

There are 5 naturally occurring stable isotopes of zinc. Three of them, 67Zn, 68Zn, and 70Zn, are in sufficiently low natural concentrations to allow enriched preparations of these isotopes to be used in tracer studies of human zinc metabolism. As with calcium, early zinc stable-isotopes studies in children generally used a single oral tracer followed by fecal collections to assess absorption used this approach to show that infant formulas may be extrinsically tagged to assess absorption in infants. More recently, Fairweather-Tait et.al., used this approach to show that zinc absorption from a vegetable-based weaning food was 30% and was not affected by iron fortification of the food. This value is similar to that reported using this technique for infant zinc absorption from a wheat-based infant cereal. (**Serfass *et.al.*, 2001)**

II. Conclusion

Mineral stable-isotope research remains a field still relatively new in its application to assessment of nutrient absorption and utilization. For magnetic sector instruments, accuracy of this technique for natural-abundance samples is 0.1–0.2% of accepted values. Recently, human nutritional research has shifted away from radioisotope use toward increased use of stable isotopes. Advances in identifying genes related to nutrient bioavailability may open up an important new role for stable isotopes. However, the availability of more facilities to perform sample analysis may remain a limiting factor in the development of this field in the near future.

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