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Short Communication

Influence of the consumption pattern of magnesium from magnesium-rich mineral water on magnesium bioavailability

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Abstract

It is generally considered that the absorption of Mg is inversely related to the ingested dose. The objective of the present study was to determine if the mode of administration (bolus *v.* consumption throughout the day) could influence Mg bioavailability from Mg-rich natural mineral water comparing the same nutritional Mg amount (126 mg). Using a 2 d cross-over design, twelve healthy men were asked to drink 1·5 litres Mg-rich mineral water either as 2 × 750 ml or 7 × 212 ml throughout the day. Two stable isotopes (^{25}Mg and ^{26}Mg) were used to label the water in order to distinguish both regimens. Fractional apparent Mg absorption was determined by faecal monitoring and Mg retention was determined by measuring urinary excretion of Mg isotopes. Higher Mg absorption (50·7 (SD 12·7) *v.* 32·4 (SD 8·1) %; $P=0·0007$) and retention (47·5 (SD 12·9) *v.* 29·0 (SD 7·5) %; $P=0·0008$) from Mg-rich mineral water were observed when it was consumed in seven servings compared with larger servings. Thus, regular water consumption throughout the day is an effective way to increase Mg bioavailability from Mg-rich mineral water.

Key words: Magnesium: Mineral water: Bioavailability

Dietary reference intakes in the USA for Mg are 400–420 mg and 310–320 mg for men and women, respectively[1]. The increase in the consumption of processed foods during the 20th century, in industrialised countries, has led to a decrease in the average daily intake of Mg from 410 mg to less than 300 mg/d. Inadequate intake and impaired absorption of Mg are thought to contribute to various pathologies in humans including osteoporosis, hypertension and atherosclerotic vascular disease, and, more recently, colon cancer[2,3]. In contrast to food, Mg-rich mineral waters may provide significant amounts of Mg without the energy. The Mg from mineral water has been previously evaluated in human subjects using stable isotopes and has been shown to be well absorbed and retained[4,5]. Nevertheless, Mg bioavailability could be affected by several factors[6]. Among them, the size of the Mg load is likely to be the most important. It has been shown in a study with three infants that fractional Mg absorption and retention was increased after distributed *v.* bolus administration of a 20 mg Mg dose[7]. The influence of the consumption pattern of Mg, i.e. distributed over the day *v.* a bolus consumption, on Mg bioavailability has never been evaluated in adult men; therefore, this was the objective of the present study using a relevant nutritional dose of Mg (126 mg) provided by an Mg-rich mineral water.

Experimental methods

Subjects

A total of twelve healthy Caucasian men aged 18–40 years were recruited from the University of Franche Comté, in Besançon, France. No medication or vitamin/mineral supplements were allowed during the study. Subjects were non-smokers and were not allowed to practise intensive sport during the duration of the study. The study was

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conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethical Committee of Besançon, France. Written informed consent was obtained from all subjects.

Study design

As shown in Fig. 1, a 2 d cross-over design was used. At 4 weeks before the Mg bioavailability evaluation, subjects consumed 1 litre Mg-rich mineral water per d (Hépar®; Nestlé Waters, Vittel, France), corresponding to a supplementary intake of 110 mg Mg/d. The aim was to homogenise Mg status of the subjects, as performed in a previous study[4]. Following this period, Mg bioavailability was evaluated using another mineral water (Contrex®; Nestlé Waters, Contrexéville, France) containing 84 mg Mg per litre. The subjects were given 1·5 litres mineral water per d for two consecutive days. Subjects were randomised to a sequence of two servings per d followed by seven servings per d, or seven servings per d followed by two servings per d. At 3 d before isotope administration, subjects began consuming a standardised diet, which was maintained until the end of the isotope feeding. Using the Genesis® R&D Nutrition Analysis program (ESHA Research, Salem, OR, USA) it was calculated that this diet provided about 10 450 kJ (2500 kcal) daily with 16 % of energy as protein, 34 % as lipid and 50 % as carbohydrate. Mg intake from the diet was 373 (SD 120) mg/d. A total dose of 2 mg of a dysprosium faecal marker ($DyCl_3$) was administered along with the stable isotopes to check the completeness of the faecal collections. At the end of the stable isotope administration, subjects received a dose of a coloured faecal marker, i.e. 100 mg brilliant blue encapsulated into gelatin to determine the end point of the faecal collection.

Sample collection

Venous blood samples were taken the day before the stable isotope administration for determination of serum total Mg concentrations. Before the study, subjects provided urine and faecal samples as reference for the baseline isotopic composition. Starting from the time of the first isotope administration, complete urine and faecal collections were performed. Complete 24 h urine collections were carried out and their volumes recorded during the 10 d following isotope administration. Faeces were collected individually for the same period of time until the complete excretion of the coloured faecal marker. All samples were frozen at −20°C until analysed.

Stable isotope labels

The two Mg stable isotopes were used in order to discriminate between the two regimens. Fasting volunteers drank either Mg-rich mineral water labelled with 30 mg Mg as $^{25}MgSO_4$ when consumed twice per d or with 30 mg $^{26}MgSO_4$ when distributed into seven servings during the day. Mg stable isotopes enriched in ^{25}Mg (99·2 %) and ^{26}Mg (99·69 %) were purchased from Chemgas (Boulogne, France) in the form of MgO. They were prepared as reported previously[4]. Isotopic enrichment and concentration of ^{25}Mg and ^{26}Mg tracer solutions were determined by inductively coupled plasma MS using an ELAN 6000 equipped with a Meinhart nebuliser and cyclonic glass spray chamber (Perkin Elmer, Rotkreuz, Switzerland).

Sample analyses

Serum Mg concentration was measured by a colorimetric method, using xylidyl blue with a multitest analyser (RA 1000; Bayer Corporation, Tarrytown, NY, USA). Intra- and inter-assay variations were 1·2 and 2·7 %, respectively. Randox human serum was used as a reference serum for quality control (RIQUAS, Randox International Quality Assessment Scheme; Randox Laboratories Ltd, Crumlin, Co. Antrim, UK).

Duplicate freeze-dried faecal samples were digested in a microwave digestion system (MDS-2000; CEM, Matthews, NC, USA). Total Mg concentration in urine and faecal samples was determined by flame atomic absorption spectrophotometry (model Z5000; Hitachi, Tokyo, Japan) using operating conditions recommended by the manufacturer. Human reference urine (Seronorm; Nycomed, Oslo, Norway) was analysed with the urine samples for quality control. Accuracy of the Mg faecal analysis was controlled by analysing the NIST SRM 1577b bovine liver (National Institute of Standards and Technology, Gaithersburg, MD, USA) as a certified

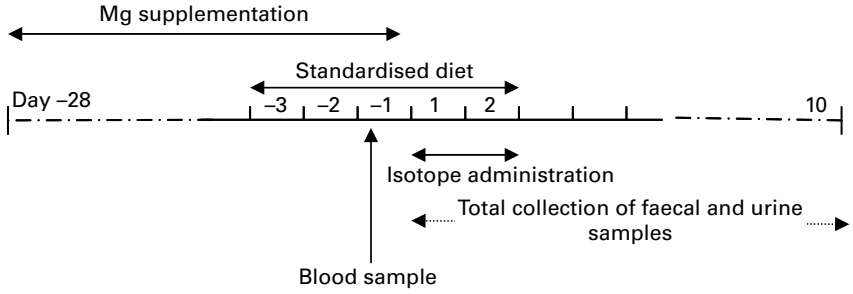

Fig. 1. Schema of the study. Before the bioavailability test, subjects were supplemented with Mg for 4 weeks with an Mg-rich mineral water (Hépar®; Nestlé Waters, Vittel, France) in order to homogenise their Mg status, which was measured through a blood sample collected on day −1. Mg bioavailability was determined from a second Mg-rich mineral water (Contrex®; Nestlé Waters, Contrexéville, France) labelled with stable isotopes, over 2 d in a cross-over design. On day 1, subjects received either two intakes of ^{25}Mg-labelled water per d or seven intakes of ^{26}Mg-labelled water, and inversely on the second day.

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reference material and a pooled faecal sample as a laboratory standard. The CV for Mg concentration in the faecal pool was 2·7 % (n 10).

Total $DyCl_3$ and Mg stable isotope ratios were determined by inductively coupled plasma MS[8]. Within-run precision for $DyCl_3$ analysis was < 1 % for faecal pool samples, 1–7 % for post-faecal samples; repeatability was < 1 % (n 5) and the limit of detection was < 1 ng/l. Within-run precision for ^{25}Mg:^{24}Mg and ^{26}Mg:^{24}Mg ratio analysis (five replicates) was 0·5–1·2 %. After correction for instrumental bias, isotope ratios for baseline urine and faecal samples were within 0·8 % of the accepted International Union of Pure and Applied Chemistry (IUPAC) values[9]. Accuracy was also verified by spiking basal urine and faecal samples with known amounts of highly enriched ^{25}Mg or ^{26}Mg. Repeatability, determined by measuring baseline samples several times over 4 h on the same day, was < 0·6 % for faeces (n 30). Limits of detection for ^{25}Mg and ^{26}Mg measurement were 0·7 and 1·9 % in faecal samples, respectively, and 0·9 % in urine for both isotopes.

Calculation and statistics

Mg isotopic ratios and total Mg concentrations of the samples were used to determine the amount of both tracers that were excreted[4]. The fractional apparent absorption was calculated (MgAA) as follows:

$$MgAA = (Do - Mo)/Do,$$

where Do is the amount of enriched oral tracer ingested and Mo is the amount of enriched oral tracer excreted in faeces. The retention of ^{25}Mg and ^{26}Mg was calculated by subtracting the total amounts of ^{25}Mg and ^{26}Mg excreted in urine and faeces from the administered dose.

Demographics and baseline characteristics were displayed and summarised globally using descriptive statistics. The apparent absorption and retention (%) were summarised descriptively for each regimen. A cross-over model with period, sequence and subject was used to test the regimen effect of Mg absorption and retention (%). This approach corrects for potential effects of test sequence on the outcome. Adjusted means for the model (covariates: sequence, period and subject), 95 % CI and P values are provided. Only subjects with good compliance for stool collection were considered in the analyses. A good compliance for stool collection was defined as a percentage of $DyCl_3$ recovery of at least 80 %. SAS (version 9.1; SAS Institute, Inc., Cary, NC, USA) was used to perform the statistical analyses. The study was powered to detect a difference of at least 10 % in the absorption between the two regimens.

Results

The study group of healthy men was aged 24·5 (SD 1·7) years (range 21–27 years). Their mean weight, height and BMI were 68·9 (SD 4·4) kg (range 60–74 kg), 176·9 (SD 5·0) cm (range 170–185 cm) and 22·0 (SD 1·0) kg/m^2 (range 20·6–23·3 kg/m^2), respectively. Before the study, mean serum total Mg concentrations were 0·83 (SD 0·05) mmol/l, ranging from 0·78 to 0·95 mmol/l. All individual values were in the normal range. Analysis of $DyCl_3$ in faeces indicated good compliance of the subjects for complete stool collection, except for one subject. Therefore, this subject was excluded from all analyses. The mean $DyCl_3$ recovery for the eleven remaining subjects was 104·8 (SD 5·5) %, with individual values ranging from 94 to 112 % of the administered dose. Mg absorption from mineral water consumed twice per d was 32·4 (SD 8·1) %. When consumed in seven servings, mean Mg absorption increased to 50·7 (SD 12·7) %. For all subjects, Mg absorption from water consumed in seven servings was higher than from water when consumed in two servings over the day, resulting in a significant increase of 18·3 (95 % CI 10·1, 26·5) % (P=0·0007), corresponding to a relative increase of 56·4 %. Mean Mg retention from 1 litre mineral water consumed twice per d was 29·0 (SD 7·5) % and increased significantly when consumed in seven servings per d to 47·5 (SD 12·9) %. The absolute increase in Mg retention was 18·5 (95 % CI 10·0, 26·9) % (P=0·0008).

Discussion

A wide range of Mg absorption values (11–76 %) have been reported in the literature. Such variability is most probably due to the Mg load than to the analytical method, the formulation or to the food matrix, which may contain enhancers or inhibitors of absorption. This was clearly demonstrated by three studies in adults, reviewed by Ekmekcioglu[10]. The upper range of Mg absorption was obtained for the lowest ingested amount of Mg. Nevertheless, the higher absolute amount of Mg absorbed was obtained with the highest ingested Mg dose. In an experiment carried out in infants, fractional absorption of Mg of the same Mg load (20 mg) was increased after distributed (64·0 (SD 3·9) %) $v.$ bolus administration (54·3 (SD 5·9) %)[7]. Thus, by modifying the consumption pattern over the day of a given Mg amount, a higher absolute quantity of Mg entered the body. Mg retention was also greater in all infants after distributed administration. Up to now, this effect has never been evaluated in adults with a relevant nutritional amount of Mg; this was the objective of the present study. A dose of 156 mg Mg (including stable isotopes), corresponding to 39 % of the RDA for men, was consumed by the study group. For all subjects, Mg absorption was significantly increased when the water was ingested over seven servings during the day, resulting in an 18 % increase of Mg available to the body. Similar observations have been reported for Ca[11]. This increase in Mg absorption after distributed $v.$ a bolus administration can most probably be explained by the absorption of low Mg amounts via the transient receptor potential ion channels (TRPM6)[12]. Accordingly, a distributed ingestion of nutritional amounts of Mg over the day would help to avoid saturation of TRPM6, and consequently increase the entrance of the mineral into the body. On the other hand, it cannot be excluded that the large volume of water consumed with the two servings decreased the transit time of Mg in the intestine. Therefore, the total Mg uptake could also have been limited by a reduced time of exposure to the site of absorption.

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Mg retention depends not only on absorption but also on homeostatic mechanisms at the level of the kidney and on Mg status. Therefore, in order to palliate any sub-Mg deficiency and to minimise differences in Mg status, subjects were supplemented for 4 weeks before the evaluation. As reported in the study carried out in infants, the present results showed that Mg retention in adult men also increased after distributed *v.* bolus administration. The absolute increase in Mg retention was 18·5 %, corresponding to a relative increase of 63·8 %. This increased retention was expected, since it is well established that plasma Mg homeostasis is controlled by the kidney. In the case of hypermagnesaemia, Mg excess is rapidly excreted via the urine, erasing or at least decreasing at the same time the efficacy of Mg supplementation. Thus, one simple means of increasing Mg absorption and retention of a given daily intake of Mg is to divide the daily dose into smaller increments taken at equally spaced intervals throughout the day. In terms of supplementation, this may result either in a more rapid repletion of body pools when deficiency or sub-deficiency occurs, or in a better prevention of the appearance of a sub-deficiency. Using this consumption pattern, Mg-rich mineral water delivers Mg more efficiently to the body. Further studies are required to confirm these results with Mg-rich foods or food supplements.

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The authors' responsibilities were as follows: M. S., J.-M. A., M. J. A., G. D. and A. B. designed the study and wrote the protocol; M. S., G. D., A. B. and A. G. were responsible for the clinical investigation; J.-M. A. and F. B. performed the statistical analysis; A. G., M. S. and P. K. A. performed the analytical parts of the study; all authors performed the research and edited the paper.

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