

Nutrition Discussion Forum

Answer to 'Health effects of sulphate'

The reaction of M. J. Arnaud, which is more a bibliographic review (67 references) than a letter, was expected. Arnaud accepts our experimental results, i.e. a higher urinary Ca excretion with a CaSO₄-rich mineral water than with milk for identical Ca intake, but he argues against our interpretation on the responsibility of sulphate.

The pertinence of many of the cited references could be criticized, but, to avoid a long and fastidious polemic, we propose a shorter response focusing on the most important points and without a list of bibliographic references, which would be redundant with the ones included in our article and/or Arnaud's letter.

Unchanged intestinal and faecal excretion

We acknowledge the limits of our study, especially concerning the metabolic balances that were not completely performed. We have explained why we avoided this arduous and expensive method, considering that the error in the 1-week calciuria measurements on thirty-seven subjects was certainly much less than in a full balance on ten subjects. The 'large individual and daily variations in the absorption' pointed out by Arnaud also apply to the other parameters of Ca metabolism, but that does not invalidate the mean values obtained on thirty-seven subjects studied in a cross-over design during 12 weeks, and they are not due to differences between milk and water. Consequently, we figured out the hypothesis that the coefficient of Ca intestinal absorption from milk or water was the same, in order to base the comparison only on urinary loss measured during periods of 7 days and not only on a sample of 24 h as in several cited studies.

Nobody contests the importance of intestinal Ca absorption and Arnaud's justifications are superfluous. The hypothesis of the same efficiency of Ca absorption from milk and water is perfectly valid, as attested by several quoted studies. Among them, the results of the study using stable isotopes performed by Couzy *et al.* (1995) in the Nestlé Research Center, which shows no difference between milk and water (Contrex), are now strangely omitted by Arnaud. The best milk Ca intestinal bioavailability suggested in the study in pigs (Pointillart *et al.* 2000) was observed in a situation of 'calcium restriction', which is not the case in our study. Moreover, if Ca absorption from milk had been significantly higher, it would have induced a higher urinary Ca excretion, whereas the opposite situation was observed.

The recent study of Spence *et al.* (2005), using metabolic balances and kinetic modelling, comparing Ca absorption and retention from two soya-protein isolates and casein-whey protein, is cited by Arnaud as evidence of an inverse relationship between

urinary and endogenous faecal Ca, with no consequence on retention. As a matter of fact, this relationship was observed in only one of the two studied soya-protein isolates and, moreover, no conclusion could be drawn using data derived from a too imprecise faecal Ca excretion in only fifteen subjects. The authors said objectively that they 'lacked the power to determine small differences in calcium retention by using the metabolic balance approach' and that 'a sample size of 180 would have been needed to observe a difference of approximately 40 mg in calcium retention'. That is precisely what we tried to emphasize in our discussion.

Sulphate intake, metabolism and acidogenic effect

A commonly accepted consensus exists to attribute a urine acidifying property to sulphate and to explain, through the oxidation of sulphur-containing amino acids, the potential effect of proteins on calciuria. Our estimation of the sulphate provided by 400 ml of milk is not overestimated. Arnaud calculates the value of 40 mg using the contents quoted by Florin *et al.* (1993). However, Florin *et al.* measured only free sulphates or sulphates released by *in vitro* acid hydrolysis, not the sulphates derived from oxidation of the sulphur in sulphur-containing amino acid. This potential intake from milk is not negligible, but is much less than the very great amount of 1180 mg of free sulphates in 1 litre of Contrex water. Indeed, other common foods and beverages contain high levels of sulphate; according to Florin *et al.*, the main contributor to sulphate intake is beer. The conclusive hypothesis of this study, occulted in the letter, is that sulphate-reducing bacteria produce potentially toxic H₂S from non-absorbed dietary sulphate, resulting in a risk of damaging the colonic epithelium. Some sulphate-rich mineral waters contain five to ten times more sulphate than beer.

We did not measure urinary sulphate and we admit this deficiency. It is well known, however, that sulphate is well absorbed and excreted in urine because this anion cannot be metabolized or retained. The absence of data on urinary sulphate does not preclude the interpretation based on the difference in sulphate intakes we forwarded.

The debate on the acidogenic sulphate action and its effect on calciuria is more complex. Arnaud recalls a study by one of us (Guéguen and Besançon, 1972) on sheep, showing a higher urinary Ca loss with sulphate than with carbonate and 'an unexplained lower bone resorption ... with sulphate'. In fact, the more important result from this radioisotopic balance study with kinetic modelling was not the reduction of resorption (–30%) but the very important reduction of bone accretion (–63%). This is in agreement with the interpretation given

by Walser and Browder (1959) for the effect of sulphate on bone and would explain why the urinary deoxyypyridinoline did not vary significantly in our study.

It is not possible, however, to extrapolate to man results obtained on animal species in which urine is not an important way for Ca excretion (rat, pig, beef cattle). The very important differences in sulphate intake pointed out by Arnaud are not exclusion factors. Actually, if sheep or rats in quoted studies consumed very high quantities of sulphates (adjusted to the weight of man), they also consumed much more of all other nutrients, notably Ca (eight to twenty times more!). For example, a 60 kg pig consumes at least 15 g Ca/d to cover its requirements, compared with less than 1 g/d in man!

The study by Roux *et al.* (2004) comparing the effect of a daily supplement of 560–605 mg Ca provided by two Ca-rich mineral waters, rich in either bicarbonate or sulphate, during 28 d, with a restricted food Ca intake (400 mg/d) in thirty-nine elderly women, is used by Arnaud to confirm the absence of negative effect of sulphate. In this interesting study, there were no Ca balances but mostly measurements of parathyroid hormone and markers of bone turnover, whereas other measurements, including calciuria, were ‘secondary endpoints’. According to the authors, the increase in urinary sulphate did not induce an ‘excess of urinary calcium’. Actually, this study was not precise enough to show small differences because measurements were done only using a unique 24 h urine collection in twenty-four women. Moreover, variability was very important, and, curiously, the urinary Ca loss did not increase whereas the Ca intake increased from 400 to 1000 mg/d, which does not allow any conclusion about small variations of calciuria. It is evident that every Ca supplement added to a Ca-restricted diet induces an improvement of bone parameters. However, this study clearly shows that the reduction of serum parathyroid hormone and the favourable effect on bone markers were much more important with the bicarbonate-rich water. Most of the studies showing a favourable effect of Ca-rich mineral waters on bone have been done with bicarbonate-rich waters. If Ca from sulphate-rich water is less retained in bone it must be excreted, and why not in the urine?

Some other studies more than 50 years old are put forward by Arnaud to show the absence of effect of CaSO₄ on Ca balance. We agree that we did not quote these studies, considering that, in order to observe small differences in calciuria, the poor sensitivity of analytical methods at that time was another limiting factor.

The absence of a measurable effect of dietary sulphate on urinary acidity is widely documented by Arnaud. We also pointed out the difficulties in achieving these measurements, directly or indirectly (water does not contain protein, P, K). However, the effect of sulphate’s acidogenic action on the urinary pH is certainly attenuated, or even corrected, by the obligatory excretion of alkaline cations. Consequently, it is not surprising that the urine acidity was affected slightly. In this respect, as previously shown, the alkaline effect of bicarbonate-rich waters gives to these beverages a better efficacy on bone mineralization.

Our explanation of the effect of sulphate on urinary Ca loss seems to be correct, even if we admit that other dietary factors present in milk and exclusively considered by Arnaud may have an influence.

The potential effects of unbalanced nutrient intakes

It is obviously difficult to equalize all nutrients intakes when comparing such a complex food as milk with a mineral water. Differences in intakes are important, notably for proteins, P and Na, and the influence of each of these factors on urinary and endogenous faecal excretion were largely documented and discussed in our article.

The influence of K was mentioned, but, as underlined rightly by Arnaud, certainly not considered sufficiently due to the lack of reliable data. The different K intake could explain a part of the calciuria difference, but certainly not entirely. With respect to the small increase in diuresis, its impact on calciuria seems to us less verified. It is difficult, when comparing very different foods, to obtain the same urinary volume, and other studies quoted as references by Arnaud did not do any better! If calciuria increases with diuresis, must it be recommended to drink less water in order to preserve bone mineral mass?

Actually, Arnaud does not contest the difference in calciuria between milk and sulphate-rich water but exonerates sulphate by explaining the advantage of milk in terms of its P and K contents. We do not share his analysis completely, but from the practical point of view, only the final result is important. The proper effect of sulphate could be verified by full metabolic balance studies comparing, with a same intake of all other nutrients, a Ca(HCO₃)₂-rich water with a CaSO₄-rich water. It is surprising that such a study has never been published, considering its scientific and applied interest!

Long-term effects on bone of the calcium sulphate-rich mineral water studied

We do not contest the interest in Ca-rich mineral waters, either bicarbonated or sulphated, for their contribution to Ca intake, which often is inadequate when the consumption of dairy products is low. As pointed out in our conclusion, ‘when the Ca intake is low, for example in the absence of milk products, the skeleton derives its Ca from all absorbable sources of Ca, including vegetables and CaSO₄-rich waters’, but we do not agree with the assimilation claims comparing Ca-rich mineral waters with milk.

Additional data (Aptel *et al.*, 1999) from the EPIDOS observational study on risk factors of hip fracture are used by Arnaud as definitive evidence of the efficiency of CaSO₄-rich mineral waters (notably Contrex and Vittel) for fracture prevention. An intake of 100 mg Ca from these two waters is linked to an increase of 0.5 % in femur bone mineral density, this increase being only 0.2 % with the other sources of Ca, including milk, but with no statistically significant difference between the waters and other Ca sources. The contribution of the two mineral waters to total Ca intake is not given in the article by Aptel *et al.*, and, in this study, only 36 % of subjects drank mineral waters only (all waters combined) and 43 % drank tap water only. The conclusion drawn from incomplete and non-significant data, that a woman drinking 1 litre of CaSO₄-rich mineral water daily would have bone mineral density equivalent to a woman 7 years younger who drinks only Ca-poor water, seems strongly questionable. Aptel *et al.* are more cautious by writing ‘calcium-rich water’ (and not ‘CaSO₄-rich water’) and

recommending this strategy 'for those who do not consume milk and dairy products'.

Conclusion

An increase in urinary Ca loss is certainly not always the reflection of an increase in the absorption, neither for milk nor for water. Other factors are involved, notably sulphates, to determine an additional obligatory urinary loss. However, the main practical objective is to provide enough Ca to reach the nutritional recommendations, and, according to nutritional surveys, Ca intake is critical in large parts of the population. We agree with Arnaud that this should be the first step and that the next one is to consider the differences in bioavailability. Nevertheless, excessive claims should not be made to compare Ca sources, particularly milk and some mineral waters. Independently of Ca metabolism, an excessive sulphate intake is questionable as further research is needed to clarify the potential deleterious effect of dietary sulphate on colonic epithelium.

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