

Acute effects of calcium citrate with or without a meal, calcium-fortified juice and a dairy product meal on serum calcium and phosphate: a randomised cross-over trial

Sarah M. Bristow*, Gregory D. Gamble, Angela Stewart, Rama Kalluru, Anne M. Horne and Ian R. Reid
Department of Medicine, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand

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Abstract

Ca supplements, but not dietary Ca, have been associated with increased cardiovascular risk. This difference could be related to differences in their acute effects on serum Ca. We therefore examined the effects of Ca from different sources on serum Ca and phosphate in a randomised, cross-over trial of ten women (mean age of 69 years). Fasting participants received a single dose of 500 mg of Ca as citrate, citrate with a meal, fortified juice or a dairy product meal, with at least 6 d between each intervention. Blood was sampled before and 1, 2, 4 and 6 h after each intervention was ingested. Serum ionised and total Ca increased significantly from baseline over 6 h. Using calcium citrate fasting as a comparator, the elevations in ionised and total Ca were similar after fortified juice, delayed after calcium citrate with a meal and smaller after a dairy product meal. Serum phosphate and calcium–phosphate product increased from baseline after calcium citrate with a meal and after a dairy product meal, and they declined after calcium citrate fasting and after fortified juice. The elevations in serum Ca in the present study were only slightly different from those observed after the administration of 1000 mg of Ca in a previous study. These data indicate that different sources of Ca have different acute effects on serum Ca and support recommendations that dietary Ca might be safer than supplements. Whether these differences contribute to differences in cardiovascular risk requires further study.

Key words: Calcium supplements: Dairy products: Fortified juice: Serum calcium

Ca supplements are widely used to treat and prevent osteoporosis; however, they have been associated with increased cardiovascular risk. In our earlier meta-analyses of randomised controlled trials of Ca supplements with or without vitamin D, allocation to Ca was associated with an increase of approximately 30% in the risk of myocardial infarction and with a smaller, non-significant increase in the risk of stroke^(1,2). A further recent meta-analysis showed a similar adverse effect of Ca alone on myocardial infarction but found no adverse effect on the broader endpoint of CHD in women, so debate in this area continues^(3–5). Several observational studies have also examined cardiovascular risk in Ca supplement users, with some studies^(6–8), but not others^(9–11), reporting an increase in risk; however, the findings of such studies are of lesser value when evidence from randomised controlled trials is available.

The mechanism by which Ca supplements could increase cardiovascular risk is currently uncertain, but it could be mediated through their acute effects on serum Ca. In observational studies, increased serum Ca concentrations have been associated with an increased risk of vascular calcification^(12,13), cardiovascular events⁽¹⁴⁾ and mortality⁽¹⁵⁾. We and others have

shown that the ingestion of a Ca supplement results in an acute elevation in serum Ca, although most subjects remain within the normal reference range^(16–21). However, a limitation of these acute studies was that a 1000 mg dose of Ca was studied, but Ca supplements are commonly taken in one or two daily doses of 500–600 mg, which might have smaller calcaemic effects. Most of the trials included in our meta-analyses of Ca supplements and cardiovascular events used twice daily dosing of Ca^(1,2).

Unlike Ca supplements, most available evidence suggests that dietary Ca intake is not associated with increased cardiovascular risk^(6,7,22). One possible difference between dietary Ca and supplemental Ca is their effects on serum Ca. Compared with supplemental Ca, dietary Ca is consumed in smaller amounts throughout the day and may be expected to have a lesser impact on serum Ca. Furthermore, even large doses of dietary Ca appear to result in smaller elevations of serum Ca than equivalent doses of supplemental Ca^(23,24), although this has not been well studied. The difference could be related to the protein and fat in dietary Ca sources slowing intestinal transit and reducing the rate at which Ca is released into the blood. If this is true, it could lead to recommendations that

*Corresponding author: S. M. Bristow, fax +64 9 923 2375, email s.bristow@auckland.ac.nz

Ca supplements be taken with meals in order to reduce their calcaemic effects⁽²⁵⁾. However, there is presently no evidence to document this difference, because acute studies of Ca supplements have administered the supplements after fasting or with a light meal^(16–19). Ca-fortified foods may also be used to supplement dietary intake. The effects of these foods on serum Ca could be similar to those of supplements^(24,26), but again, this has not been well studied.

Because it is possible that the adverse cardiovascular risk associated with Ca supplements is related to their effects on serum Ca, the calcaemic effects of different Ca sources are of interest. We carried out a cross-over trial which examined the acute effects of 500 mg of calcium citrate on serum Ca and whether these were different when calcium citrate was taken with a meal containing protein and fat or when Ca was obtained from fortified juice or a meal of dairy products. We also examined changes in serum phosphate in the present study, seeing as phosphate influences Ca metabolism and calcium–phosphate product has been associated with cardiovascular risk⁽²⁷⁾. However, the interventions were not designed to be balanced for phosphate content.

Methods

Participants

The participants in the present study were ten women who were at least 5 years postmenopause. We studied only women because most of the participants in the meta-analyses in which an adverse cardiovascular effect of Ca supplements was identified were female^(1,2), and postmenopausal women are the greatest users of Ca supplements⁽²⁸⁾. We recruited women from among those who had participated in a previous study by our group which examined the acute effects of 1000 mg of Ca on serum Ca⁽²¹⁾. A total of thirty women were contacted by mail and invited to participate in the present study, and ten agreed to do so. All of the women had already met the inclusion and exclusion criteria for our previous trial. In brief, we included women if they were 5 or more years postmenopause. We excluded women if they had a past history of CHD, cerebrovascular disease or peripheral vascular disease, renal impairment, chronic liver disease or any other concurrent major systemic illness, including malignancy, had used Ca supplements in the previous 6 months (including as part of our previous study), were currently using calciferol supplements of more than 2000 IU/d (50 µg/d), had used bisphosphonates in the previous 2 years, had hormone replacement therapy in the previous 12 months or were using any other medication known to affect Ca or bone metabolism.

Protocol

Participants attended four 6 h sessions at our research clinic, with each session separated by at least 6 d. During each session, participants arrived at the clinic the morning after an overnight fast. A baseline blood sample was collected, after which participants immediately received one of the following

four treatments through random assignment: 500 mg of Ca as citrate (citrate-fasting); 500 mg of Ca as citrate taken immediately after a meal (citrate-with-a-meal); 500 mg of Ca from a Ca-fortified fruit juice (fortified-juice); or 500 mg of Ca from a meal of unfortified dairy products (dairy-meal). A randomisation schedule was prepared by staff who were not in contact with the participants. For each participant, a computer-generated random number was given to each session, and the sessions were then sorted by random number. The lowest number was allocated to citrate-fasting, the next lowest to citrate-with-a-meal, then fortified-juice and then the dairy-meal. The four interventions and their composition are described in Table 1. A combination of dairy products, rather than a single food, was used as the dairy-meal in order to best represent a normal meal. The Ca-fortified juice was a commercially available product fortified with Ca as lactate and gluconate (Schweppes Australia Pty Ltd.). Calcium citrate (Jost Chemical Company) was purchased from Hawkins Watts and administered as a powder in capsules. Blood samples were collected 1, 2, 4 and 6 h after each treatment was ingested. A light breakfast meal was provided 1 h after the citrate-fasting and fortified-juice interventions. A light lunch (toast with jam, honey or marmalade and tinned fruit in juice) was provided 4 h after all interventions were ingested. The lunch contributed a further 73 mg of Ca and 142 mg of P. All of the meals were served after the blood sampling procedures were complete for that time point. Water was allowed *ad libitum*, but no other food or drink was permitted. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all of the procedures involving human subjects were approved by the Northern A Health and Disability Ethics Committee. Written informed consent was obtained from all subjects. The present study was registered with the Australia New Zealand Clinical Trials Registry (ACTRN12614000342617).

Measurements

Serum ionised Ca was measured on anaerobically handled specimens using an ABL800 FLEX blood gas analyser (Radiometer). Samples for the measurement of total Ca and phosphate were batch analysed at the end of each 6 h session using a Cobas modular analyser (Roche Diagnostics). Calcium–phosphate product (i.e. the product of Ca × phosphate) was calculated using ionised Ca and phosphate. Parathyroid hormone and markers of bone turnover were not assessed in the present study, because eating itself impacts parathyroid hormone and bone turnover^(29,30), and the interventions were balanced only in Ca content. Body weight was measured using electronic scales, and height was measured using a Harpenden stadiometer (Holtain Limited). Dietary Ca was assessed using a validated FFQ⁽³¹⁾.

Statistical analyses

The study was powered (80% power at the 5% significance level for a two-tailed test) to detect differences of at least 1 SD in serum Ca between pairwise comparisons made in the



Table 1. Composition of the interventions

Intervention and meal*	Serving size	Ca (mg)†	P (mg)†	Fat (g)†	Protein (g)†	Carbohydrate (g)†
Citrate-fasting						
Calcium citrate	500 mg	500				
1 h after the ingestion of calcium citrate						
Wheat bread	84 g	64	118	2.2	7.6	27
Peaches in juice	115 g	7	20	0.1	0.7	10
Total		571	138	2.3	8.3	37
Fortified-juice						
Ca-fortified fruit juice	500 ml	500	40	0.1	1.5	53
1 h after the ingestion of fortified juice						
Wheat bread	84 g	64	118	2.2	7.6	27
Peaches in juice	115 g	7	20	0.1	0.7	10
Total		571	178	2.4	9.8	90
Citrate-with-a-meal						
Calcium citrate	500 mg	500				
Eggs	2 eggs	58	212	10.6	13.6	0.4
Ham	50 g	0	34	2.6	8.4	1
Wheat bread	42 g	32	59	1.1	3.8	13
Margarine	20 g	2	2	14	0	0
Total		592	307	28.3	25.8	14.4
Dairy-meal						
Milk	100 ml	128	96	1.5	3.5	9.6
Sweetened yogurt	125 g	158	138	3.6	5	15
Cheddar cheese	34 g	230	193	12.2	8.4	0.1
Wheat bread	84 g	64	118	2.2	7.6	27
Total		580	545	19.5	24.5	51.7

* All meals were served with an option of jam, marmalade or honey as well as decaffeinated tea or coffee without milk, which would have contributed an additional 2 mg of Ca and 4 mg of P.

† Calculated from the nutrition label or, if not available, from the New Zealand Food Composition Tables⁽⁴³⁾.

same individuals. The mean baseline values and standard deviations were calculated from the baseline measurement at the first visit as being representative of the time 0 h values at each visit. Data were analysed on an intention-to-treat basis using a mixed models approach to repeated measures (Proc Mixed, SAS version 9.2; SAS Institute, Inc.). The change from baseline (calculated from the individual changes from individual baseline values) was the dependent variable, and the baseline value of the appropriate variable was included as a covariate (ANCOVA). Significant main (time or treatment allocation) and interaction effects (time × treatment allocation) were further explored using Tukey's method to construct honestly significant differences; however, because these comparisons were pre-planned, the pairwise *P* values were not further adjusted for multiplicity.

Results

The characteristics of the participants are presented in Table 2. Changes in ionised Ca over 6 h are presented in Fig. 1 and changes in total Ca in Fig. 2. Ionised and total Ca increased from baseline after each intervention. Ionised Ca was higher than baseline between 2 and 6 h after citrate-fasting (all time points *P*<0.0004) and fortified-juice (all *P*<0.0001), at 4 and 6 h after citrate-with-a-meal (all *P*<0.003) and at 2 and 4 h after the dairy-meal (all *P*<0.04). Total Ca was higher than baseline between 1 and 6 h after citrate-fasting (all *P*<0.02), fortified-juice (all *P*<0.0001) and the dairy-meal (all *P*<0.05) and between 2 and 6 h after citrate-with-a-meal (all *P*<0.0001). Differences in the changes in serum Ca between the interventions are shown in Figs. 1 and 2.

Compared with citrate-fasting, the rise in both ionised and total Ca after citrate-with-a-meal was delayed but not diminished in extent. Fortified-juice was indistinguishable from citrate-fasting for both indices. The dairy-meal generally caused smaller increases in serum Ca than did citrate-fasting.

Changes in serum phosphate are presented in Fig. 3. Citrate-fasting and fortified-juice tended to reduce serum phosphate concentrations. Phosphate was lower than baseline at 2 and 4 h after citrate-fasting (all *P*<0.03) and between 1 and 4 h after fortified-juice (all *P*<0.03). Citrate-with-a-meal had the opposite effect – phosphate was increased from baseline at 4 h (*P*=0.0002). After the dairy-meal, the phosphate changes were biphasic, lower than baseline at 1 and 2 h (all *P*<0.005)

Table 2. Baseline characteristics of participants

(Mean values and standard deviations, *n* 10)

	Mean	SD
Clinical characteristics		
Age (years)	69	3
Weight (kg)	74	13
Height (m)	1.63	0.06
Dietary Ca (mg/d)	840	400
Biochemical characteristics		
Ionised Ca (mmol/l; normal range: 1.15–1.30 mmol/l)*†	1.24	0.03
Total Ca (mmol/l; normal range: 2.10–2.55 mmol/l)*†	2.25	0.05
Phosphate (mmol/l; normal range: 0.70–1.50 mmol/l)*†	1.08	0.11

* Normal range from laboratory where the measurements were performed.

† Mean baseline values and standard deviations were calculated from the baseline measurement at the first visit as being representative of the time 0 h values at each visit.

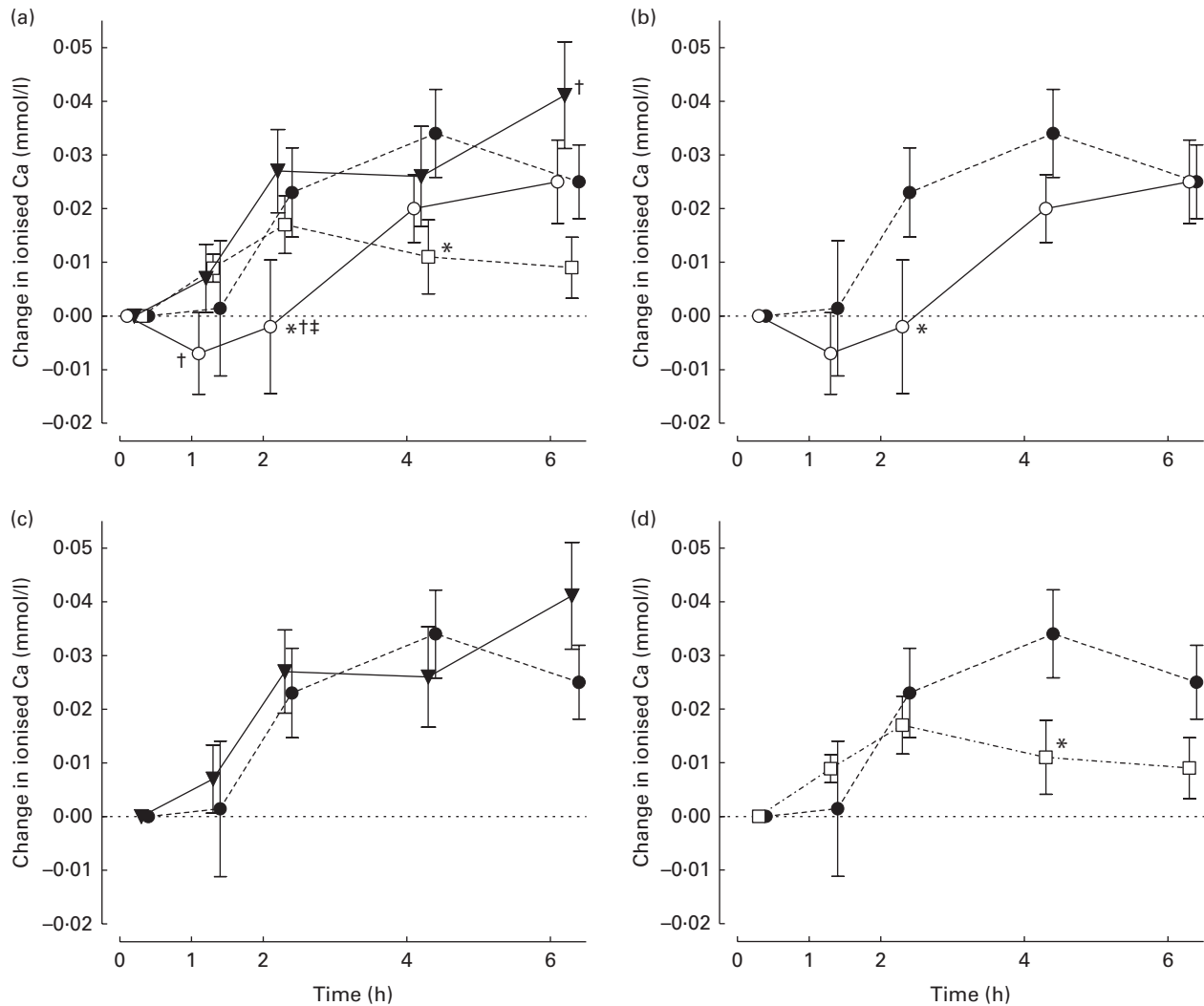


Fig. 1. Changes in serum ionised calcium in postmenopausal women (n 10) over 6 h after the ingestion of 500 mg of calcium as citrate when fasting (citrate-fasting, ●), citrate with a meal (citrate-with-a-meal, ○), calcium-fortified juice (fortified-juice, ▼) or a dairy product meal (dairy-meal, □). (a) Changes after all interventions are shown. To facilitate comparisons, (b–d) changes after citrate-with-a-meal, fortified-juice and the dairy-meal compared with citrate-fasting are shown. Values are means, with their standard errors represented by vertical bars. There was a significant difference in the change in ionised calcium between the treatments ($P=0.04$; ANCOVA, treatment \times time interaction). * Mean value was significantly different from that of citrate-fasting ($P<0.05$); † Mean value was significantly different from that of the dairy-meal ($P<0.05$); ‡ Mean value was significantly different from that of fortified-juice ($P<0.05$).

but increased from baseline at 4 h ($P=0.0001$). Changes in serum calcium–phosphate product are presented in Fig. 4 and followed a similar time course to the changes in serum phosphate.

To determine whether changes in Ca are dose-related, we compared the changes in serum Ca after 500 mg of Ca as citrate in the present study with the effects of 1000 mg of Ca as citrate or carbonate in our previous study⁽²¹⁾. The changes in ionised and total Ca are presented in Fig. 5. Changes in ionised Ca were similar between the interventions, but the change in total Ca was smaller after 500 mg of Ca as compared to 1000 mg of Ca. When we restricted the analysis to only the five women who took part in both studies and had been randomised to citrate or carbonate in the previous study, the changes in serum ionised and total Ca were not different, although the CI were large (data not shown).

Discussion

In the present study, serum ionised and total Ca increased from baseline over 6 h following the ingestion of Ca from all sources. Compared with citrate-fasting, the increases in ionised and total Ca tended to be similar after fortified-juice, delayed after citrate-with-a-meal and smaller after the dairy-meal. Serum Ca remained elevated for up to 6 h after the citrate-fasting, citrate-with-a-meal and fortified-juice interventions, which suggests that two doses of 500 mg of Ca daily could result in some elevation in serum Ca for 12 or more hours each day. Although serum Ca remained within the normal range, the greatest increases in ionised and total Ca (0.03 and 0.08 mmol/l, respectively, after citrate-with-a-meal) were equivalent to 1–1.6 SD of baseline values. In observational studies, differences of 1 SD in serum Ca within the

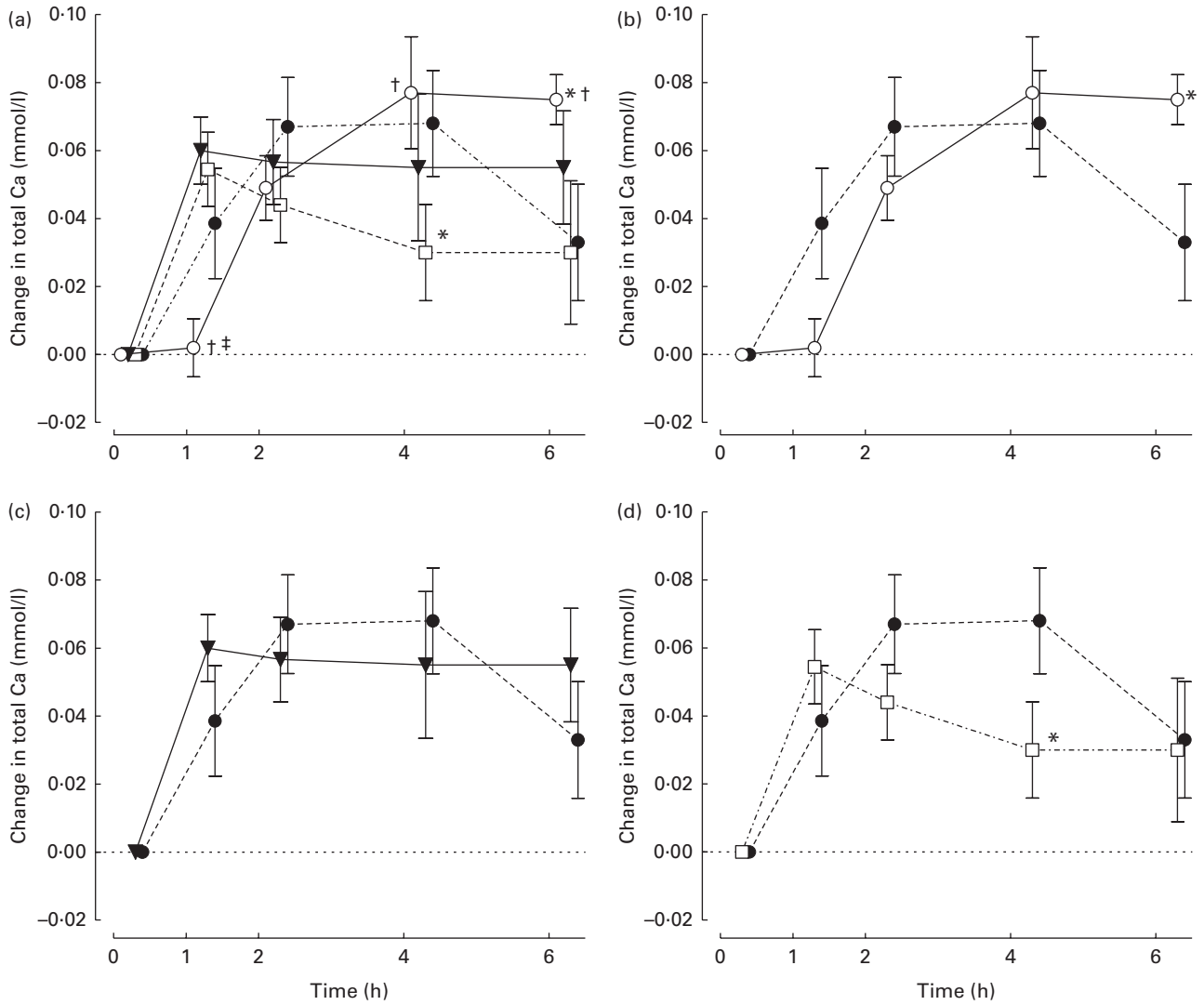


Fig. 2. Changes in serum total calcium in postmenopausal women (n 10) over 6 h after the ingestion of 500 mg of calcium as citrate when fasting (citrate-fasting, ●), citrate with a meal (citrate-with-a-meal, ○), calcium-fortified juice (fortified-juice, ▼) or a dairy product meal (dairy-meal, □). (a) Changes after all interventions are shown. To facilitate comparisons, (b–d) changes after citrate-with-a-meal, fortified-juice and the dairy-meal compared with citrate-fasting are shown. Values are means, with their standard errors represented by vertical bars. There was a significant difference in the change in total calcium between the treatments ($P=0.004$; ANCOVA, treatment \times time interaction). * Mean value was significantly different from that of citrate-fasting ($P<0.05$). † Mean value was significantly different from that of dairy-meal ($P<0.05$). ‡ Mean value was significantly different from that of fortified-juice ($P<0.05$).

normal range have been associated with a 17% increase in the risk of a cardiovascular event⁽¹⁴⁾ and a 30% increase in the risk of coronary artery calcification⁽¹³⁾.

The changes in ionised Ca were similar and changes in total Ca were slightly smaller after 500 mg of Ca as citrate in the present study in comparison to 1000 mg of Ca as citrate or carbonate (with a light meal) in our previous study⁽²¹⁾. Similarly, investigators reported only slight differences in serum ionised Ca after 500 *v.* 1500 mg of Ca⁽³²⁾. This could be explained by saturation of the Ca absorption mechanism at these doses. In one study, urinary Ca increased rapidly after the ingestion of 200 and 500 mg Ca doses, with only small additional increases after 1000 and 2000 mg doses⁽³³⁾. This might explain the lack of a dose–response relationship between Ca supplements and cardiovascular risk. In a reanalysis of the Women’s

Health Initiative, our group reported that Ca supplements (1000 mg/d) increased cardiovascular risk only among women who were not already taking personal Ca supplements⁽²⁾. Among those already using personal Ca supplements, allocation to Ca did not further increase cardiovascular risk.

Unlike Ca supplements, most available evidence suggests that high intakes of dietary Ca do not increase cardiovascular risk^(6,7,22), although one study reported an increase in risk at intakes of more than 1400 mg/d⁽¹¹⁾. A key difference between supplemental and dietary Ca could lie in their effects on serum Ca, but few studies had examined this and none had done so after a normal mixed-meal. In a study in nine young women, ionised Ca increased after 400 mg of Ca from a supplement or from cheese but not after Ca from milk, sesame seeds or spinach⁽²³⁾. In a study in nineteen young men and women,

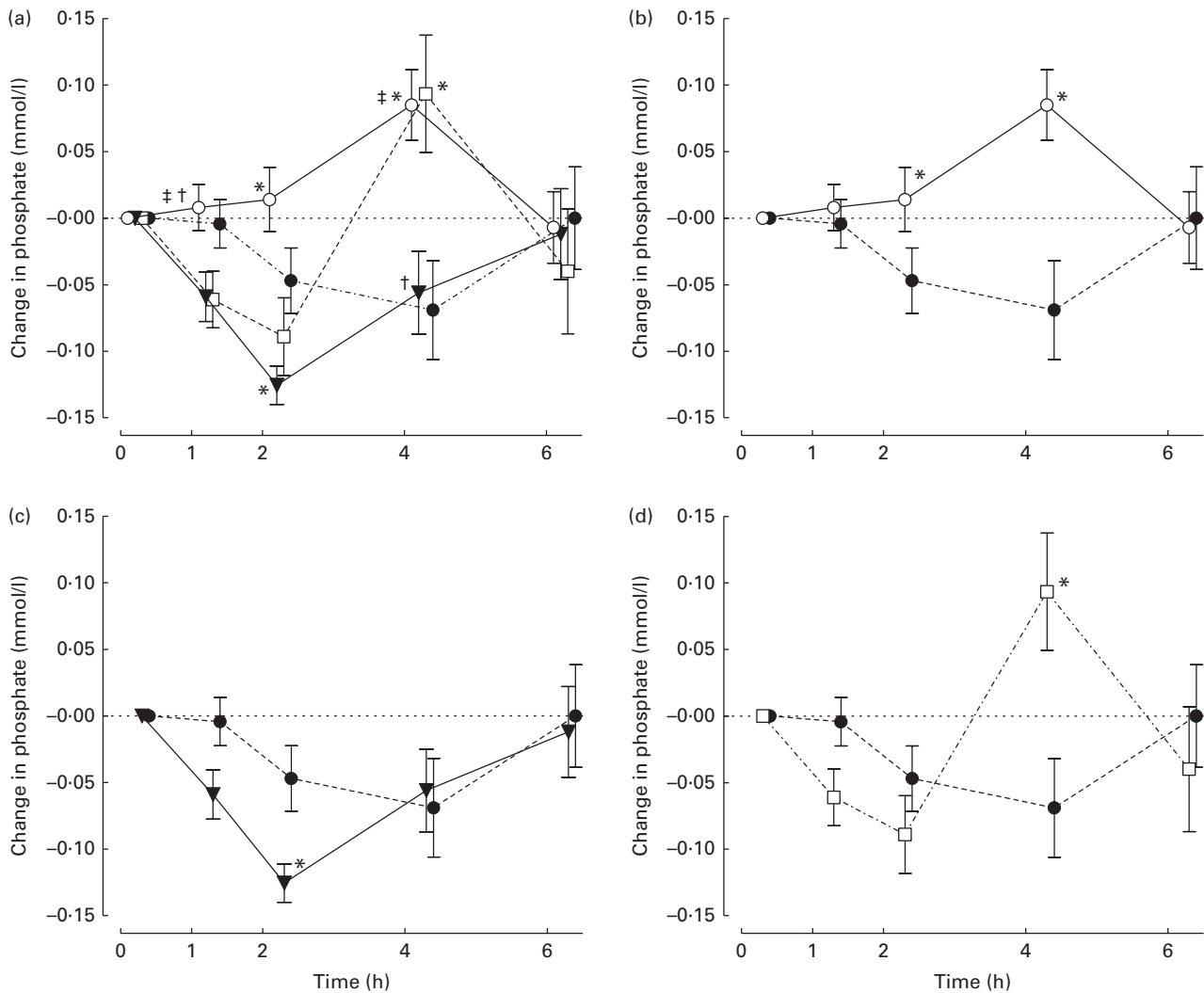


Fig. 3. Changes in serum phosphate in postmenopausal women (n 10) over 6 h after the ingestion of 500 mg of calcium as citrate when fasting (citrate-fasting, ●), citrate with a meal (citrate-with-a-meal, ○), calcium-fortified juice (fortified-juice, ▼) or a dairy product meal (dairy-meal, □). (a) Changes after all interventions are shown. To facilitate comparisons, (b–d) changes after citrate-with-a-meal, fortified-juice and the dairy-meal compared with citrate-fasting are shown. Values are means, with their standard errors represented by vertical bars. There was a significant difference in the change in phosphate between the treatments ($P < 0.0001$; ANCOVA, treatment \times time interaction). * Mean value was significantly different from that of citrate-fasting ($P < 0.05$); † Mean value was significantly different from that of the dairy-meal ($P < 0.05$). ‡ Mean value was significantly different from that of fortified-juice ($P < 0.05$).

500 mg of Ca from unfortified milk resulted in a smaller increase in ionised Ca over 4 h than did Ca-fortified powdered milk, Ca-fortified yogurt and a calcium carbonate supplement⁽²⁴⁾. Similarly, we observed a smaller elevation in serum Ca at some time points after a dairy-meal as compared to citrate-fasting, citrate-with-a-meal and fortified-juice. Moreover, Ca from the diet is usually consumed in amounts that are less than 500 mg, so the resulting elevations in serum Ca are likely to be even smaller than those reported here.

The smaller elevation in serum Ca following the dairy-meal may indicate a lower bioavailability of Ca. However, Ca from dairy products has been shown to be as well absorbed as Ca from supplements⁽³⁴⁾. Therefore, the co-ingested protein and fat in dairy products may delay gastric emptying and intestinal transit, thereby reducing the rate at which Ca is released into the blood. However, the citrate-with-a-meal intervention had

similar protein and fat content to the dairy-meal, but it resulted in a different excursion in serum Ca. Therefore, the smaller calcaemic effect of dairy products appears to be related in part to other factors, including perhaps the distribution of Ca throughout the food or the chemical form of Ca. For example, milk fortified with dairy Ca has been shown to elevate serum Ca less than milk fortified with calcium carbonate⁽³⁵⁾.

The increase in serum Ca was delayed by 1–2 h after citrate-with-a-meal as compared to citrate-fasting. This likely reflects a delay in gastric emptying and intestinal transit after the meal. At 6 h, total Ca was greater after citrate-with-a-meal as compared to citrate-fasting, which suggests that Ca absorption was improved by the meal. The absorption of even highly soluble Ca salts is improved when they are taken with a meal⁽³⁶⁾. Ionised Ca was not different between the citrate-with-a-meal and citrate-juice interventions at 6 h. Because ionised Ca

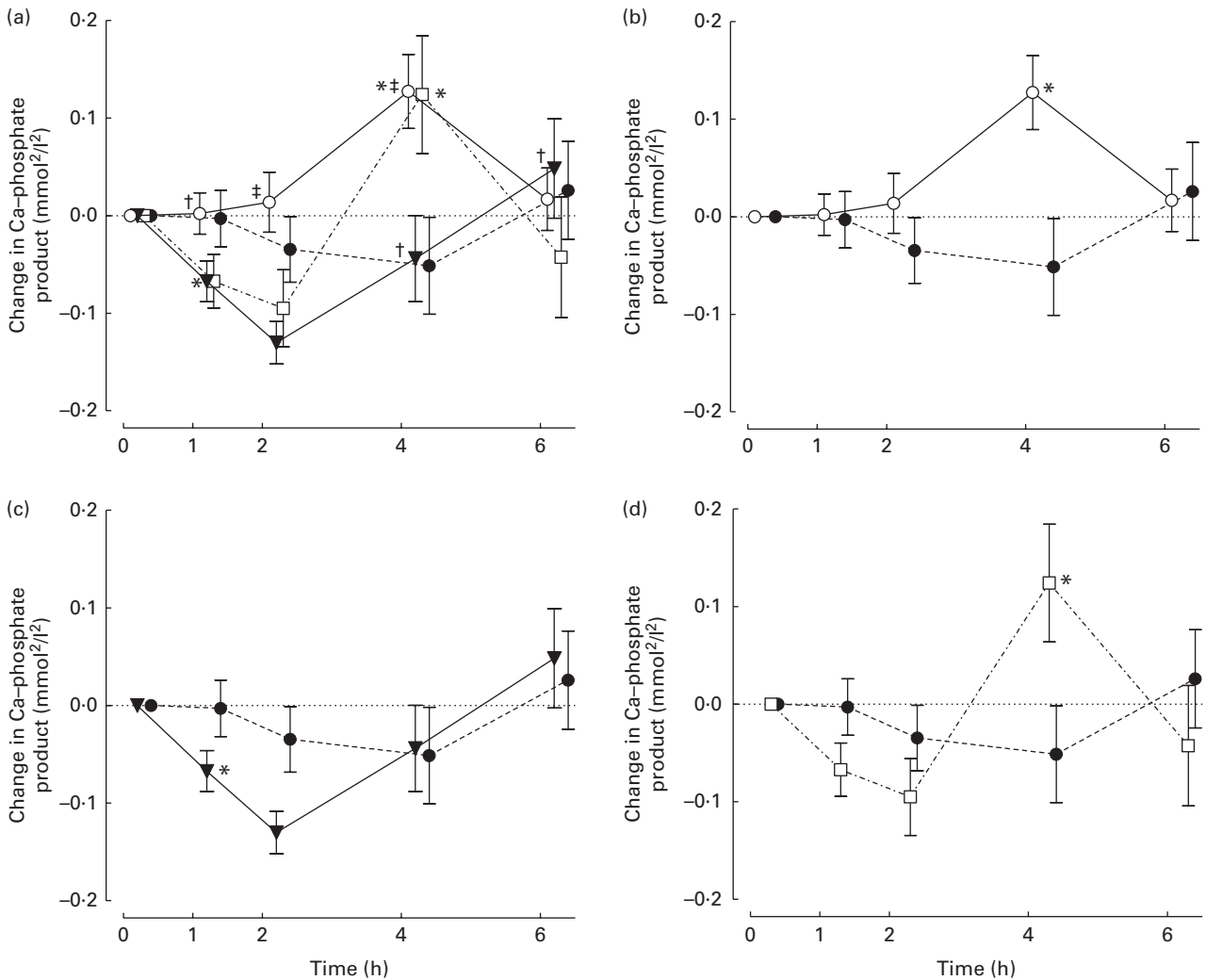


Fig. 4. Changes in serum calcium–phosphate product in postmenopausal women (n 10) over 6 h after the ingestion of 500 mg of calcium as citrate when fasting (citrate-fasting, ●), citrate with a meal (citrate-with-a-meal, ○), calcium-fortified juice (fortified-juice, ▼) or a dairy product meal (dairy-meal, □). (a) Changes after all interventions are shown. To facilitate comparisons, (b–d) changes after citrate-with-a-meal, fortified-juice and the dairy-meal compared with citrate-fasting are shown. Values are means, with their standard errors represented by vertical bars. There was a significant difference in the change in phosphate between the treatments ($P=0.0002$; ANCOVA, treatment \times time interaction). * Mean value was significantly different from that of citrate-fasting ($P<0.05$). † Mean value was significantly different from that of the dairy-meal ($P<0.05$). ‡ Mean value was significantly different from that of fortified-juice ($P<0.05$).

appeared to be rising between 4 and 6 h, it is possible the peak elevation in ionised Ca after citrate-with-a-meal was missed. Alternatively, increased serum phosphate after citrate-with-a-meal may have lowered the ionised Ca concentration. The similar elevation in ionised Ca at 6 h and the greater elevation in total Ca at that time point suggest that the rise in serum Ca is not reduced by taking supplements with meals. Thus, changes in serum Ca in individuals who consume Ca supplements alongside their regular diet are likely to be at least as great as those observed in acute dosing studies (in which supplements are usually administered after fasting or with a light meal).

The citrate-with-a-meal and dairy-meal interventions had a higher phosphate content than the other interventions, and they consequently resulted in an increase in serum phosphate and calcium–phosphate product at 4 h. Increased serum

phosphate and calcium–phosphate product have been associated with cardiovascular risk in the general population^(27,37,38). Although serum phosphate and calcium–phosphate product increased after citrate-with-a-meal, there was a similar increase in both parameters following the dairy-meal, and high intakes of dairy products do not appear to increase cardiovascular risk⁽⁶⁾. Phosphate declined at 2 h from baseline after citrate-fasting, fortified-juice and the dairy-meal but not after citrate-with-a-meal. This was probably a result of the higher carbohydrate content of these meals, seeing as carbohydrates after a fast result in the movement of phosphate into cells⁽³⁹⁾.

The mechanism by which repeated elevations in serum Ca that are within the normal range could increase cardiovascular risk is presently uncertain, but several possibilities exist (for a more in-depth review, see Reid *et al.*⁽⁴⁰⁾). These effects could be mediated through the Ca-sensing receptor. Changes

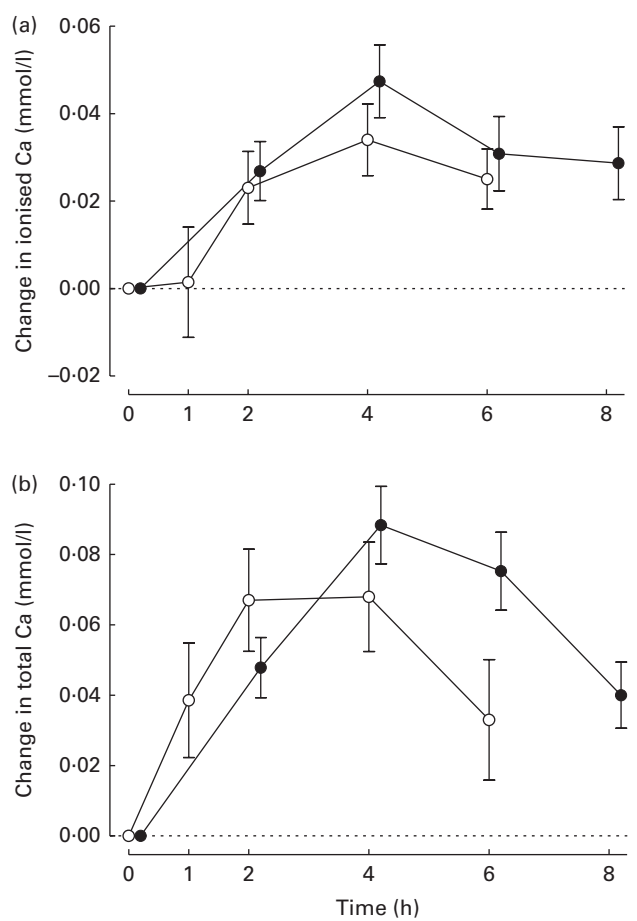


Fig. 5. Changes in (a) serum ionised calcium and (b) serum total calcium in postmenopausal women after 500 mg of calcium as citrate (—○—) when fasting between 1 and 6 h (*n* 10) and 1000 mg of calcium as citrate or carbonate (—●—) with a light meal between 2 and 8 h (*n* 40). Data for the change after 1000 mg of calcium are from a previous study⁽²¹⁾. Values are means, with their standard errors represented by vertical bars. There was no significant difference in the change in ionised calcium between the interventions at corresponding time points ($P=0.47$; ANCOVA, treatment \times time interaction). There was a significant difference in the change in total calcium between the interventions at corresponding time points ($P=0.015$). On *post hoc* testing, the difference in the change in total calcium was not significant at any individual time point.

in serum Ca of the magnitude in the present study profoundly impact parathyroid hormone secretion⁽²¹⁾, which indicates that Ca-sensing receptor activation has occurred. Increased serum Ca concentrations could influence vascular calcification, perhaps by activating the Ca-sensing receptor on vascular cells or by altering the balance between the promoters and inhibitors of calcification, such as pyrophosphate and fetuin-A. Serum Ca could also influence the tendency of blood to clot, given that Ca is essential for several components of the coagulation cascade and platelets express the Ca-sensing receptor. An effect on blood pressure is also possible, seeing as acute increases in serum Ca have been associated with transient elevations in blood pressure^(41,42).

Only women were included in the present study because most of the participants ($\geq 83\%$) were female in the meta-analyses in which an adverse cardiovascular effect of Ca

supplements was identified^(1,2), and postmenopausal women are the greatest users of Ca supplements⁽²⁸⁾. No interaction by sex was found in these meta-analyses, which suggests that Ca supplements have a similar effect on cardiovascular risk in both men and women. Future studies should examine the acute calcaemic effects of different Ca sources in men. Furthermore, the acute effects of Ca sources may be different from those reported here among different age or ethnic groups or among those with reduced renal function because of potential differences in Ca absorption and/or excretion. The form of Ca salt that is administered may also determine its calcaemic effects; however, we have previously shown that changes in serum Ca are similar after calcium citrate and calcium carbonate⁽²¹⁾, which suggests that the changes observed in the present study will apply to most commonly used supplements.

In summary, 500 mg of Ca as citrate, fortified juice or a dairy product meal significantly increased serum Ca from baseline over 6 h. The elevation in serum Ca after 500 mg of Ca as citrate was only slightly different from that after 1000 mg of Ca as citrate or carbonate. Ca-fortified juice had a similar effect on serum Ca as a Ca supplement when taken in an equivalent dose. Taking a Ca supplement after a meal containing protein and fat appeared to only delay the elevation in serum Ca, not to diminish it. Ca obtained from a meal of dairy products resulted in a smaller elevation in serum Ca than Ca from a supplement. With self-selected diets, this contrast may be even more marked, seeing as Ca from the diet is likely to be consumed in individual helpings that are much smaller than 500 mg. This difference might explain the apparent difference between the cardiovascular effects of Ca supplements and those of dietary Ca. Further research is needed to determine how elevations in serum Ca could influence cardiovascular health.

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The authors have no conflicts of interest.

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