

RESEARCH LETTER

The effect of vitamins and minerals enriched milk on blood pressure in mildly hypertensive subjects

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In a randomized controlled study, we found no effect of a dairy drink containing additional amounts of potassium, calcium, magnesium, selenium and vitamins C and E on blood pressure (BP). The results of this study confirm the discrepancy between dietary intervention studies showing reasonable BP lowering effects and intervention studies with a combination of minerals or vitamins showing no effect. Future studies should focus on assessing the effect of subsets of combinations of minerals and vitamins in natural matrices to get a better understanding of the possible antagonistic action between some of these ingredients.

The Dietary Approaches to Stop Hypertension (DASH) study showed an impressive reduction on BP.¹ The effective components of this diet probably include minerals and vitamins. Several meta-analyses and intervention studies investigated the relationship between individual minerals and vitamins and their effect on BP. A meta-analysis showed a significant effect of potassium supplementation on systolic blood pressure (SBP) of -3.11 mm Hg and of diastolic blood pressure (DBP) of -1.97 mm Hg.² Studies on the effect of a combination of minerals^{3–6} and vitamins⁷ showed mixed results. The present study is, to the best of our knowledge, the first study investigating the effect of a combination of minerals and vitamins on BP.

We tested the BP lowering effect of skimmed milk with added vitamins and minerals (calcium 446 mg, magnesium 100 mg, selenium 40 μ g, vitamin C 180 mg, vitamin E 30 mg and tocopherol equivalents and either of two levels of potassium (high-K combination 1500 mg/serving and low-K combination 750 mg/serving)) in an 8 week trial. Untreated subjects with elevated BP were enrolled. The placebo and the run-in product consisted of 250 g of water. By adding titaniumoxide, xanthan and pectin, the appearance of the placebo product was comparable to the other test products. No BP effects have been described for these additives. Products were provided in nontransparent cups and lids. Office BP was measured three times with an oscillometric automatic device (OMRON HEM-907) following an overnight fast and after 15 min of rest.

The mean of the second and third measurement was used for statistics. Office BP was measured at 2 days at baseline (week 0) and at the end of the intervention (week 8), and once at week 2, week 4, and after 2 weeks of wash-out. Twenty-four hours ambulatory blood pressure (24 h ABP) was measured once at baseline and at week 8 using an oscillometric automatic device (Spacelab monitor type 90217). Body weight and 24 h urinary sodium and potassium excretion were measured at baseline and week 8. The primary outcome of this study was the reduction in SBP. Secondary outcomes included DBP and 24 h ABP. The target sample size of 40 subjects per treatment group was estimated to provide 80% power and $\alpha=0.05$ (one-sided) to detect a reduction in SBP of 5 mm Hg. Data are expressed as mean \pm s.e.m. Analyses were performed using analysis of variance. To compare differences between groups, the Tukey multiple comparison method was used. A total of 124 subjects completed the study. Data of nine subjects were excluded (use of medication interfering with BP ($n=5$), the uptake of the product ($n=1$), arrhythmia ($n=1$) and other ($n=2$)). Baseline characteristics (BP levels, body weight and urinary excretion levels) were comparable in each of the groups. After 8 weeks, office SBP decreased by 4.6 ± 1.4 (high-K combination), 4.5 ± 1.4 (low-K combination) and 5.1 ± 1.4 mm Hg (placebo). These changes were not significantly different between the groups. The decrease in office DBP, pulse pressure (PP), 24 h SBP, 24 h DBP and HR were not significantly different either (for more information about office DBP and PP data see Table 1). Office BP levels after 2 weeks of wash-out did not change significantly when compared to values at week 8. Body weight showed an increase in the intervention groups compared to baseline, while it showed a decrease in the placebo group. There was, however, no interaction between weight change and intervention group on BP changes. At the end of treatment, sodium excretion increased somewhat in the high-K combination group and urinary potassium excretion increased during treatment, depending on the potassium content in the product.

The results found in the present study are in contrast with many studies addressing interventions with the individual components. One explanation for this may be that the amount of minerals and vitamins

Table 1 Office SBP, DBP and PP (mean \pm s.e.m.)

	<i>Placebo</i>	<i>High-K combination</i>	<i>Low-K combination</i>
<i>Office SBP</i>			
Week 0	143.1 \pm 1.4	145.4 \pm 1.8	144.2 \pm 1.8
Week 8	139.4 \pm 1.8	141.5 \pm 1.7	140.4 \pm 1.7
<i>Office DBP</i>			
Week 0	84.9 \pm 1.2	85.4 \pm 1.6	87.8 \pm 1.2
Week 8	83.0 \pm 1.4	84.0 \pm 1.3	86.9 \pm 1.2
<i>PP</i>			
Week 0	58.3 \pm 1.4	60.0 \pm 1.7	56.5 \pm 1.5
Week 8	56.4 \pm 1.3	57.5 \pm 1.6	53.5 \pm 1.2

Abbreviations: DBP, diastolic blood pressure; PP, pulse pressure; SBP, systolic blood pressure.

in the intervention products used in this study is smaller than the amounts usually tested.^{2,8–10} Studies exploring the effect of combinations of minerals or vitamins on BP, hypothesized that the reductions would be greater than the effect reported in studies of each mineral/vitamin alone.^{3–7} However, although most of these studies have shown a decrease in BP, they did not find a clear additive or synergistic effect of the nutrients. Notably, in two studies, in which supplements of combinations of minerals were given to the subjects, the effect found was even lower than expected from one of the minerals (that is potassium).^{4,5} As an explanation for these unexpected findings, the possibility of a counteracting effect of the combination of minerals on the effect of potassium on BP was mentioned.⁵ This phenomenon might have influenced the results of our study as well.

The results of the present study are also in contrast with the substantial effects found in dietary intervention studies. Several aspects might explain this difference. First, studies replacing complete diets not only add potentially beneficial components, but reduce potential negative components in the diet as well. Second, there may be other components in foods 'not known' yet to be beneficial for BP, which are unchanged in supplementation trials, but are higher in studies replacing (part of) a diet. Finally, nutrients in dietary supplements/products may not reduce BP to the same extent as nutrients in food because of altered bioavailability. The dairy matrix used in this study may be not the optimal matrix for the nutrients to show their effect.

The question now is whether or not to continue exploring the efficacy of mineral and vitamin supplements/products on BP. In the PREMIER study, the effect of the DASH diet was explored when subjects purchased their own food. The effect found was much smaller than expected. One of the explanations mentioned was that subjects in real life do not fully comply to the guidelines.¹¹ This illustrates that it is hard to change someone's diet and difficult to extrapolate findings from well-controlled studies and motivated volunteers to the

population at large. Therefore, supplements or products containing a combination of nutrients resulting in a reasonable BP reduction in combination with guidelines for a healthy diet could help many people with slightly elevated BP levels, and may have a substantial impact on the total number of cardiovascular disease in Westernized societies.¹²

In conclusion, we were not able to demonstrate a BP lowering effect of a vitamin and mineral combination drink. Future studies should focus on assessing the effect of subsets of combinations of minerals and vitamins in natural matrices to get a better understanding of the possible antagonistic action between some of these ingredients.

What is known about this topic:

- Several meta-analyses and intervention studies have shown a beneficial effect of individual minerals and vitamins on BP.
- Studies exploring the effect of combinations of minerals on BP could not prove clear additive or synergistic effects. The same counts for studies exploring the effect of combinations of vitamins on BP whereas dietary intervention studies did find substantial BP lowering results, for example, the DASH diet.
- The effect of a dairy product enriched in vitamins and minerals on BP has not been tested before.

What this study adds:

- In this randomized double-blind placebo-controlled parallel study, we did not find a BP lowering effect of a dairy drink containing an additional amount of potassium, calcium, magnesium, selenium and the vitamins C and E.
- The results of this study confirm the discrepancy in results between dietary intervention studies and intervention studies with a combination of minerals or vitamins and do not suggest an additive BP effect of combinations of vitamins and/or minerals.

Conflicts of interest

LAJ van Mierlo, HCM van der Knaap, MMG Koning and J Kloek are working at the Unilever Food & Health Research Institute, Vlaardingen, The Netherlands.

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