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COMPARISON OF DIFFERENT FORMS OF CALCIUM ON BLOOD PRESSURE OF NORMOTENSIVE YOUNG MALES

Abstract
Two forms of calcium, calcium gluconate and a hydrolysed yeast, were compared with a placebo yeast for their effect on the supine blood pressure of three groups of normotensive males, ages 19-24. Calcium was supplemented at 500 mg/day in the form of calcium gluconate or calcium yeast for a period of 7 weeks and the blood pressure measured periodically. A yeast containing no calcium was given as a placebo. There was no significant change in the systolic pressure in any group during the study. After 7 weeks, there was no significant change in the diastolic blood pressure of the calcium gluconate and placebo yeast groups. The calcium yeast group had a 8.2% decrease ($p<0.01$) in diastolic blood pressure at the end of the study. The greater effectiveness of the calcium yeast as compared with calcium gluconate was a result of its greater absorption as determined by a urine excretion study. The calcium yeast produced no undesirable side effects and was the most suitable form of calcium for long term supplementation.

Introduction

There is now considerable evidence from animal studies [1, 2] and human epidemiological studies using data from the Hanes I survey [3-5] that there exists an inverse correlation between dietary calcium intake and blood pressure. Recent calcium supplementation in humans has shown that calcium carbonate and/or calcium lactate gluconate significantly lowered diastolic blood pressure in young adults [6], normal pregnant women[7] and hypertensives [8]. However, the dosage level, 1-2 g of calcium/day produced in some individuals an undesirable feeling of bloating. Heavy advertising campaigns promoting the use of calcium and media coverage of the scientific reports will undoubtedly increase the use of calcium supplements.

Calcium carbonate is the most common form of calcium found in over the counter preparations because it is the least expensive form. In order for absorption to occur, calcium carbonate must be converted to its soluble chloride in the stomach. This absorption process is impaired in elderly women who suffer from a decrease in gastric acid secretion [9]. It is precisely this group, post-menopausal women, who are prone to osteoporosis and thus need extra calcium [10]. Elderly subjects, both men and women, have a lower absorption of calcium than younger individuals and are more likely to take antacids and diuretics both of which promote a negative calcium balance [11]. There is thus a need for a calcium supplement whose absorption does not depend on the gastric secretion of acid and which does not produce undesirable side effects.
In an effort to find a more suitable regimen, we have undertaken a pilot study to investigate the effect on human blood pressure of two soluble forms of calcium, a calcium yeast and calcium gluconate, at a dose which is designed to minimise side effects.

Materials and Methods

Fifteen healthy normotensive male college students, ages 19-24 volunteered for the blood pressure study with informed consent. The study was approved by the University Human Subjects Committee. Subjects were randomly divided into three groups before testing. A 7 day dietary recall indicated that the subjects consumed an average of 599 ± 316 mg of calcium/day. This is slightly lower than the national average for this age group which is 881 ± 608 mg/day [12]. Blood pressures were taken by a trained individual with each subject in the supine dorsal position after 5 minutes rest. A double-aurical stethoscope and a mercury column sphygmanometer were used for the measurements. The reproducibility of the measurement of systolic and diastolic blood pressure was 1 mm of Hg. Prior to the supplementation period, blood pressure were taken over a period of a week in order to acclimatise the subjects.

The calcium gluconate used for this study was reagent grade from Fisher Chemical Company. The placebo and calcium yeast were grown in a nutritional media containing water, starch and protein, and in the case of the calcium yeast, calcium chloride. The yeasts are hydrolysed with proteases and the calcium yeast contains 74.19% protein with a major amino acids composition of glycine 19.87%, glutamic acid 5.82%, alanine 5.38% and aspartic acid 5.32%. The calcium yeast contains 5.20% calcium and the placebo yeast <0.05% calcium as determined by ashing and atomic absorption analysis.

The placebo yeast group took daily 4 tablespoons of the yeast. The experimental yeast group ingested 4 tablespoons of the calcium yeast (500 mg of calcium). The experimental gluconate group took 2 tablespoons per day of calcium gluconate (500 mg of calcium). The subjects ingested these powders as suspensions in milk, tea, soft drinks or fruit juices, compliance was monitored by weighing the supplement containers periodically. Five replicate blood pressure readings, both diastolic and systolic, were measured for each subject at 0, 1, 2, 3, 5, 6 and 7 weeks for calcium supplements and 0, 3 and 7 weeks placebo. The blood pressure technician and the subjects were not aware of which regimen was being taken.

Four males, ages 20-29, volunteered for the urinary excretion study with informed consent. They were asked to refrain from dairy foods during the course of the 2 week study. After one week of consuming no dairy products, the subjects appeared in the morning to receive their collection vessel. A 24 hour pre-dose urine was then collected. The next morning the subjects appeared for testing after breakfast. Each subject consumed 500 mg of calcium in the form of either the calcium yeast of calcium gluconate. The calcium was consumed in 200 ml of orange juice. A post-dose 24 hour urine was then collected. One week later the other form of calcium was taken in a random crossover design. The urines were collected over 10 ml of hydrochloric acid and refrigerated until analysis. The volumes of the samples were measured and aliquots were analysed by atomic absorption spectrophotometry after dilution with 0.5% lanthanum nitrate.

Statistical analysis was accomplished with the aid of Minitab system, version 5.1, at the University of Scranton Computing Centre. A value of $p<0.05$ was considered significant.

Results

The blood pressure data is shown in Table 1. The baseline data is the result of averaging two measurements taken a week apart before supplementation began. Although the calcium yeast group had a higher mean baseline diastolic and systolic blood pressure than the other groups, the difference was not significant using one way analysis of variance testing. There was no significant change in systolic pressure for any of the groups following supplementation. The calcium yeast group was the only group to undergo a significant change in diastolic blood pressure as a result of supplementation.

Table 1: Mean (± SD) initial and final blood pressures (BP) following 7 weeks of supplementation with 500 mg of calcium.

	Diastolic BP (mm Hg)		Systolic BP (mm Hg)	
Supplement	Initial	Final	Initial	Final
Placebo Yeast (n=5)	72.3 (3.5)	71.7 (2.0)	114.0 (3.5)	112.7 (8.2)
Calcium Yeast (n=5)	77.5 (4.9)	71.6* (2.8)	119.3 (3.4)	120.4 (7.0)
Calcium Gluconate (n=4)	74.7 (5.5)	74.1 (3.7)	114.9 (3.7)	120.6 (6.6)

* Significantly different from the initial value as measured by a paired student's t-test (p=0.023).

The temporal changes in systolic and diastolic blood pressures for the three groups are shown in Figures 1 and 2. The blood pressure results are expressed as per cent change from the baseline values in order to normalise the data and allow for a more accurate comparison of the groups. The changes are quite small for the systolic blood pressures in Figure 1 with the largest change being a +5.6% increase for the gluconate group after 6 weeks. However none of the groups are significantly different from the other at any time as measured by one way analysis of variance. The results in Figure 2 for the diastolic pressures show much larger changes ranging from +2.5% for the placebo yeast group after 7 weeks to -10.9% for the calcium yeast groups occurred after 5 weeks. However the only significant differences between the groups occurred after 7 weeks when the calcium yeast group was found to have a significantly greater change, -8.2%, in diastolic blood pressure than either the placebo yeast or diastolic blood pressure than either the placebo yeast or calcium gluconate group.

The results of the urine excretion study are shown in Table 2. All of the four subjects had a greater excretion of calcium after consuming the calcium yeast as compared to the calcium gluconate. On average the calcium yeast produced a three fold greater excretion of calcium but the results are not quite significant, p=0.06 by a paired student's t-test.

Table 2: Net twenty four urine excretion (post-dose - pre-dose) of calcium following ingestion of 500 mg of calcium in the form of calcium gluconate and calcium yeast.

Subject	Calcium Gluconate (mg Calcium)	Calcium Yeast (mg Calcium)
1	57	96
2	49	104
3	31	92
4	5	160
Mean (± SD)	35.5 (23.1)	113.0 (31.7)

Figure 1: Systolic blood pressure as mean per cent change in relation to baseline value, following supplementation with 500 mg of calcium.

Figure 2: Diastolic blood pressure as mean per cent change in relation to baseline value, following supplementation with 500 mg of calcium. *$p<0.01$ calcium yeast compared to placebo yeast, $p<0.05$ calcium yeast compared to calcium gluconate.

Discussion

A calcium supplementation period of 7 weeks was selected for this study as Belizan and Villar [6] found that the blood pressures stabilised after 7 weeks in young men supplemented with calcium carbonate plus calcium lactate gluconate. As shown in Figures 1 and 2, the systolic and diastolic blood pressure of the placebo yeast, calcium yeast and calcium gluconate were relatively stable during the 6 to 7 week period indicating homeostasis had occurred.

A low dose of calcium, 500 mg/day, was used in this study in order to minimise side effects. However all of the subjects in the gluconate group complained of gastrointestinal distress and one of the original five subjects left the study after 3 weeks. The placebo and calcium yeasts produced few complaints and all subjects completed the study with excellent compliance. The bitter taste of the yeast was well masked by consumption in beverages with a strong flavour such as fruit juices.

A previous report [6] showed that 1 g of calcium/day in the forms of calcium carbonate plus calcium lactate gluconate reduced the diastolic blood pressure of young men aged 21-24 an average of 9.0% after 7 weeks of supplementation and did not affect systolic blood pressure. Our results indicate that 500 mg/day of calcium in a similar form, calcium gluconate, did not significantly affect diastolic or systolic blood pressure of young men in a comparable age group. However, calcium yeast was effective at this lower dose and decreased the diastolic blood pressure an average of 8.2%, which is very similar to the decrease produced by the higher dosage of calcium carbonate and calcium lactate gluconate.

The mechanism for the greater effectiveness of calcium yeast compared to calcium gluconate in lowering diastolic blood pressure was investigated by means of a urinary excretion study. It has been shown that 24 hour urinary calcium excretion parallels calcium absorption in young males with low to high calcium intakes [13]. The present study indicates that the calcium yeast was more absorbed than the calcium gluconate, but the difference was not quite significant due to the small number of subjects.

This pilot study has demonstrated the effectiveness of a daily supplement of 500 mg of a calcium in the form of calcium yeast in lowering the diastolic blood pressure of normal young males. A larger clinical study is needed to determine the efficacy of the calcium yeast in the targeted population; namely, hypertensives and the elderly.

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