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A RANDOMIZED, DOUBLE-MASKED, PLACEBO-CONTROLLED STUDY OF THE EFFECTS OF CHROMIUM PICOLINATE SUPPLEMENTATION ON BODY COMPOSITION: A REPLICATION AND EXTENSION OF A PREVIOUS STUDY

GILBERT R. KAATS,[1] KENNETH BLUM,[2] DENNIS PULLIN,[3] SAMUEL C. KEITH,[1] AND ROBERT WOOD[4]

[1]Health and Medical Research Foundation, San Antonio, [2]Department of Biological Sciences, University of North Texas, Denton, [3]Sports Medicine Institute, Baylor College of Medicine, Houston, and [4]Department of Computing Resources, University of Texas Health Sciences Center at San Antonio, San Antonio, Texas

ABSTRACT

A previous study using a randomized, double-masked, placebo-controlled design found that supplementation with a minimum of 200 µg of chromium (in the form of chromium picolinate [CrP]) per day can lead to significant improvement in body composition (as measured by underwater testing using the displacement method). The present study used a similar design in which 122 subjects were randomized to receive either CrP 400 µg (n = 62) or placebo (n = 60). To control caloric intake and expenditure (which was not done in the first study), participants were required to monitor and maintain a log of their daily physical activity and caloric intake. Dual energy x-ray absorptiometry measurements were taken before and after the 90-day period. Analysis of the prestudy data for the two groups revealed no significant differences in any of the initial body composition variables studied. After controlling for differences in caloric intake and expenditure, as compared with the placebo group, subjects in the active treatment group lost significantly more weight (7.79 kg vs 1.81 kg, respectively) and fat mass (7.71 kg vs 1.53 kg, respectively), and had a greater reduction in percent body fat (6.30% vs 1.20%, respectively) without any loss of fat-free mass. A more conservative analysis of covariance revealed similar and statistically significant reductions in percent body fat and fat mass without any loss of fat-free mass. It was concluded that this study replicated earlier findings that supplementation with CrP can lead to significant improvements in body composition. *Key words:* chromium picolinate, body composition, fat mass, fat-free mass, dual energy x-ray absorptiometry.

INTRODUCTION

In a previous publication,[1] the authors summarized their research on dietary chromium, an essential nutrient, reporting that its value in human nutrition has been documented conclusively.[2] They suggested that com-

Address correspondence to: Gilbert R. Kaats, PhD, Director, Health and Medical Research Foundation, 4900 Broadway, San Antonio, TX 78209.
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bining chromium with picolinic acid in the form of chromium picolinate (CrP) could increase the bioavailability of CrP[3–7] and, therefore, improve insulin use. Because the deposition of body fat appears to be regulated to some extent by insulin,[8] the authors reasoned that improvements in insulin use could lead to reductions in fat deposition. Enhancing the effects of insulin can also have positive effects on muscle tissue, because insulin directs amino acids into muscle cells where they are assembled into proteins through the effect of insulin on the cell's genetic material. Insulin also slows the breakdown or catabolism of body protein, with a net effect of increasing the protein available for building tissue. Because chromium is a cofactor to insulin, supplemental chromium offers the potential of facilitating the maintenance or addition of fat-free mass (FFM).[9] Hence, if CrP can lower insulin resistance, it can improve body composition, because insulin resistance or deficiency results in impaired entry of glucose and amino acids into muscle cells, increased catabolism of muscle protein, and the potential acceleration of lipid deposition.[10,11]

To test these hypotheses, in the previous study[1] the authors used a randomized, double-masked, placebo-controlled protocol in which participants completed underwater testing (displacement method) at the beginning and end of a 72-day study. During the study, subjects consumed either 0 μg, 200 μg, or 400 μg of CrP per day. Results of that study showed a significant improvement in body composition with CrP supplementation, with a specific reduction in excess body fat.

In addition to determining whether the body composition changes observed in the initial study could be replicated in this study, we sought to answer three methodologic issues raised by the reviewers of the previous manuscript: (1) Because supplementation with CrP affects appetite, metabolism, and daily activity levels, would the same results be achieved if differences in caloric intake and energy expenditure were controlled or factored out? (2) Would the results be replicated with other measures of body composition, such as dual energy x-ray absorptiometry (DEXA), which are at least as precise as underwater testing but less dependent on the subject's performance and practice effects on the unusual task of exhaling before going underwater? and (3) Because the relatively high dropout rate in the first study (29.7%) could have biased the findings through selective attrition, would these same results occur if methods were used to decrease the dropout rate?

To answer these questions, we controlled for differences in physical activity and caloric intake, used DEXA testing to determine body composition, and used a methodologic technique to reduce the dropout rate.

SUBJECTS AND METHODS

Subjects

A total of 130 subjects were enrolled in the study, 122 (93.8%; 17 men

and 105 women; mean age, 42.3 years) of whom completed the testing. Subjects were recruited from a variety of fitness and athletic clubs in San Antonio and Houston, Texas, by fitness instructors and sales personnel who provided information about the study to club members who either participated themselves or recruited friends or relatives to participate. In most cases, the fitness instructors were paid to monitor the subjects as they progressed through the study to ensure that the subjects reported their physical activity levels and caloric intake (tracked the data) and completed the testing. All subjects were asked to consult with their personal physician before giving written informed consent.

Testing Equipment: Dual Energy X-Ray Absorptiometry

A number of studies have shown that DEXA can accurately measure fat and lean content in meat samples and animal carcasses[12–15] and that DEXA measurements of actual skeletal mass and total body calcium correlate highly with those taken by neutron activation analysis,[16] with a typical precision error for total body bone mineral content <1%.[17] DEXA has also been shown to be a precise method for assessing body composition in obese and nonobese subjects.[18,19] DEXA correlates highly with underwater weighing,[20] deuterium dilution,[21] and total body potassium.[22] The reliability of DEXA makes it possible to monitor the effects of relatively short-term dietary restrictions and exercise on both regional and total body composition.[23,24] A recent review of the research on DEXA has led one reviewer to conclude that DEXA is among the most accurate instruments available today for critically analyzing body composition.[25]

DEXA provides a three-compartment model of body composition: fat, lean tissue mass, and bone mineral content. Measurements are made using a constant potential energy source at 78 kVp and a K-edge filter (cerium) to achieve a congruent, stable, dual-energy beam with effective energies of 40 and 70 keV. The unit performs a series of transverse scans moving from head to toe at 1-cm intervals; the area being scanned is approximately 60 × 200 cm. Data are collected for about 120 pixel elements per transverse, with each pixel approximately 5 × 10 mm. Total body measurements are completed in 10 to 20 minutes with a scan speed of 16 cm/s, or in 20 minutes with a scan speed of 8 cm/s. The R value (ratio of low- to high-energy attenuation in soft tissue) ranges from 1.2 to 1.4.[26]

Procedure

To minimize the dropout rate, subjects were asked before signing the informed consent form, to provide a $100 deposit by check or credit card, which would not be processed unless the subject failed to complete the last DEXA test and end-of-study questionnaire. Participants were advised that return of their deposit was based solely on their completing the last tests

no matter how well or poorly they adhered to the research protocol, as long as they reported candidly on how much or how little they complied.

After completing an initial DEXA test, subjects were provided with a report of their test results and randomly assigned a number from 1 to 130, which corresponded to a bottle containing capsules with 400 μg of CrP or placebo. None of the investigators, research technicians dispensing the product, or participants knew which subject number corresponded to the placebo or active product. An independent local pharmacist acted as trustee for the study and randomly assigned subject numbers to bottles that had been prelabeled with either an "X" or "Y" to correspond with either active product or placebo.

Participants were provided with a workbook outlining the general procedures for estimating caloric intake, nutritional information for common foods, and a log for calculating and recording daily calorie balances. To monitor and adjust for differences in energy expenditure through physical activity throughout their waking hours, all subjects wore a pedometer (same method as used in previous studies[27–29]) that reflected the number of steps they took during each day or the step equivalents for activities in which it was impractical to wear the unit. Subjects recorded the total number of steps taken each day in the same daily log used to record their caloric intake, which was subsequently used to adjust the subject's net change in body fat by using the following formula: ±3500 calories = a change of 1 lb of body fat. Subjects checked in at the research center on a weekly basis to obtain a scale weight and to report their weekly physical activity levels, estimated caloric intake, and any adverse effects (none were reported).

On completion of the study and when all data were gathered and entered in the computer system, the trustee opened an envelope supplied by the manufacturer indicating which product was active and subsequently notified the senior investigator (GRK). All information was analyzed by the Department of Computing Resources at the University of Texas Health Sciences Center at San Antonio, San Antonio, Texas, under the supervision of the second author (KB). At the conclusion of the test period, subjects completed the last body composition test, were provided with their test results and deposit checks, and were asked to report how many of the capsules were consumed each day as a cross-check of the amount of product used. A subsequent analysis of these data revealed that among participants receiving CrP, the average amount consumed was 357 μg/d.

Statistical Analysis

Comparisons were made between body composition variables for the two groups at baseline using a two-tailed Student's *t* test and between

baseline and post tests for both groups using paired t-test analyses. Comparisons of changes in body composition variables from baseline to post study were made using analysis of covariance (ANCOVA), which allows differences in body composition changes between the two groups to be adjusted statistically for individual differences in caloric intake and expenditure. Both caloric intake and expenditure were used as covariants irrespective of whether or not they were significant. A final statistical analysis was conducted using a direct adjustment of the data for caloric intake and expenditure and using Student's t test between the two groups. Finally, comparisons were made between the changes occurring in the two groups without making any adjustments for caloric intake or expenditure. All data analyses were conducted at the University of Texas Health Sciences Center's Department of Computing Resources.

RESULTS

Of the 130 subjects who were recruited for this study, only 8 failed to complete the final test: 1 subject became pregnant and was asked to withdraw from the study, 3 moved from the area, 1 was ill during the posttesting period, and 3 were lost to follow-up. A comparison of the 122 subjects who completed the study with the 8 subjects who did not revealed no significant differences in any of the body composition variables.

Baseline characteristics for the 122 subjects who completed the study are provided in Table I. No statistically significant differences in baseline characteristics were observed between the active treatment and placebo groups, suggesting that the randomization process was successful in providing two equivalent groups of subjects. Table II presents a comparison of the within (baseline-ending) and between-group changes that occurred in body composition variables in both the active treatment and placebo groups over the test period. Both groups experienced significant within-group reductions in scale weight ($P < 0.001$), percent fat ($P < 0.001$), and fat mass ($P < 0.001$), although no statistically significant changes occurred in fat-free mass in either group. A comparison of the between-group changes revealed that, although the active treatment group achieved greater improvement in all body composition variables, the differences in fat-mass reduction was the only change that reached statistical significance ($P = 0.023$).

Using an ANCOVA to equate the groups for caloric intake and energy expenditure, supplementation with CrP had an even greater significant and positive effect on percent body fat ($P = 0.03$) and fat mass ($P = 0.01$), although the differences in scale weight and FFM did not reach statistical significance. ANCOVA's statistical adjustment of the data is based on calculated relationships between the variables and is a conservative statistic that is insensitive to small changes. An alternative analysis is to apply the

Table I. Mean (±SD) baseline demographic data for 122 subjects randomized to receive either chromium picolinate (CrP) (n = 62) or placebo (n = 60).

	Age (y)	Weight (kg)	Body Fat (%)	Body-Mass Index (kg/m^2)
CrP (400 µg/d)	41.1 ± 10.5	85.5 ± 23.0	42.4 ± 8.3	30.2 ± 7.1
Placebo	43.5 ± 7.6	79.9 ± 20.4	41.8 ± 6.7	28.4 ± 5.4

corrections for caloric intake and energy expenditure directly to the data and then use Student's *t* test to examine the differences between the two groups. These analyses are presented in Table III. Using this approach revealed even greater differences between the two groups, suggesting that, as compared with the placebo group, the group receiving the active treatment had a significant reduction in scale weight (7.79 kg; $P < 0.001$), percent body fat (6.30%; $P < 0.001$), and fat mass (7.71 kg; $P < 0.001$). As with ANCOVA, no statistically significant differences in FFM were observed in either group. Thus, regardless of the statistical approach used, the findings from this study are highly consistent with, and provide a replication of, the findings from our previous study as well as a recent study of the effects of CrP supplementation in swimmers.[30]

DISCUSSION

It has been proposed that the positive effect of CrP on body composition is through its ability to improve insulin use, thereby reducing fat deposition and improving entry of glucose and amino acids into muscle cells. Although the present study did not attempt to test this assertion, the findings are consistent with this hypothesis, as are the findings of a recent study[31] of the lipogenic and antilipolytic effects of insulin in human adipocytes.

Table II. Within- and between-group comparisons of mean changes (±SD) in baseline and end-of-study body composition variables for subjects receiving either chromium picolinate (CrP) (n = 62) or placebo (n = 60) during a 90-day test period.

	Weight (kg)	Body fat (%)	Fat Mass (kg)	Fat-Free Mass (kg)
CrP (400 µg/d)	−2.88 ± 3.50	−2.07 ± 3.20	−2.81 ± 3.20	−0.07 ± 2.20
*P**	<0.001	<0.001	<0.001	=0.793
Placebo	−1.81 ± 2.99	−1.20 ± 2.90	−1.53 ± 2.80	−0.29 ± 2.00
*P**	<0.001	=0.002	<0.001	=0.265
CrP versus Placebo *P*†	=0.240	=0.120	=0.023	=0.568

* Student's *t* test for repeated measures.
† Student's *t* test for independent samples.

Table III. Within- and between-group comparisons of mean changes (±SD) in baseline and end-of-study body composition variables for subjects receiving either chromium picolinate (CrP) (n = 62) or placebo (n = 60) during a 90-day test period. All data are adjusted statistically for differences in caloric intake and expenditure.

	Weight (kg)	Body Fat (%)	Fat Mass (kg)	Fat-Free Mass (kg)
CrP (400 µg/d)	−7.79 ± 9.70	−6.30 ± 9.7	−7.71 ± 9.50	−0.07 ± 2.20
*P**	<0.001	<0.001	<0.001	=0.568
Placebo	−1.81 ± 2.99	−1.20 ± 2.9	−1.53 ± 2.80	−0.29 ± 2.00
*P**	<0.001	=0.002	<0.001	=0.265
CrP versus Placebo *P*†	<0.001	<0.001	<0.001	=0.568

* Student's *t* test for repeated measures.
† Student's *t* test for independent samples.

These researchers found that CrP completely reversed insulin stimulation of fatty acid synthase activity. They concluded that, "Since fatty acid synthase is a key enzyme in de novo lipogenesis, this reflects a coordinated activation of lipolysis and inhibition of lipogenesis with CrP treatment . . . thereby inhibiting insulin-mediated triglyceride storage."[31]

In the present study, the greatest changes in body composition were the result of reductions in body fat as revealed through DEXA. DEXA testing is one of the few technologies for measuring body composition that provides a direct physical measurement of adipose tissue. Hydrostatic testing, as well as most other measures of body composition, rely on estimating a person's body fat on the assumption that body density reflects the same percentage of fat as found in cadaver studies used to validate densitometry.[32] Furthermore, even hydrostatic testing does not actually measure a person's body volume to calculate body density—it estimates body volume from scale weights obtained in and out of water. Thus, even with hydrostatic weighing, body fat is derived from two different estimates, not from a physical measurement of adipose tissue. Of course, estimates derived from hydrostatic testing can be affected by the person's ability to exhale air consistently while under water as well as variations in lung volume over time, even when exhalation is consistent.

DEXA testing resolves these difficulties because obtaining the measurement requires that the person lie still on an open testing table for 15 to 20 minutes while the body is scanned. DEXA would seem to be the preferred technology to use, because it is critical to reduce the variability in testing when attempting to measure the efficacy of products or programs that produce relatively small changes in body composition.

In the present study, no dropouts biased the results. The requirement for subjects to provide a conditionally refundable deposit appears to have made a dramatic difference in the number of subjects who completed the

final testing, negating the need to use statistical controls, such as intention to treat. Poststudy critique revealed that subjects viewed the requirement to provide a deposit as reasonable, and such a requirement may have eliminated subjects whose motivation to complete the final tests was minimal. Although the data are not definitive, the deposit requirement appears to be an effective technique for obtaining final test data and is worthy of further study.

The requirement for subjects to provide a conditionally refundable deposit was based on the subject completing the study and an end-of-study questionnaire and had nothing to do with how little or how much the participant complied with the protocol. An equal number of subjects failing to take the product in the placebo and active treatment groups does not, of course, balance the effects across the groups. For example, a subject who fails to take a product in the placebo group would have no effect on the outcome measures because a placebo does not contain the active ingredient. However, failure of a subject to take a product in the active treatment group would attenuate the effects that the active product could be having. In fact, a completely noncompliant subject in an active treatment group would actually be a placebo subject. Thus lack of compliance would, by its very nature, attenuate differences between the two groups, stressing the need to obtain accurate data on how much of a product a subject consumed. The use of weekly check-ins and personal monitoring appears to have provided more comprehensive data and reduced the amount of bias that a lack of compliance could have on the outcome measures.

CONCLUSION

The findings of the present study suggest that supplementation with CrP each day can lead to significant improvements in body composition, particularly when the changes are corrected for differences in caloric intake and expenditure. In addition, the results of this study replicate the findings of a previous study, which suggest that the improvements observed are evident with both underwater and DEXA testing technologies. Finally, because an unusually high number of subjects (93.8%) completed the final testing, requiring research subjects to provide a conditionally refundable deposit (to be returned on completion of final testing) is a technique worthy of further study.

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