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THE EFFECT OF A HIGH CHROMIUM YEAST ON THE BLOOD GLUCOSE CONTROL AND BLOOD LIPIDS OF NORMAL AND DIABETIC HUMAN SUBJECTS

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ABSTRACT

A new high potency organic chromium yeast was investigated for its effect on blood glucose control and serum lipids in a group of 23 normal and diabetic subjects which were sub-divided into normals, hyperglycemics, insulin-dependent diabetics and non-insulin dependent diabetics. Each volunteer daily took 100 mg of yeast containing 218 μg of chromium for a period of six months. The blood and serum was analyzed before supplementation and periodically throughout the study. Transient improvements in the various parameters occurred in all of the groups in the early portion of the study. However, after six months of supplementation, the only group to statistically significantly benefit was the hyperglycemic group. This group had improved blood glucose control, lowered serum lipids and a decreased risk of coronary heart disease.

INTRODUCTION

Chromium has been recognized as an essential trace element for both animal and human nutrition. Recently, the National Academy of Sciences/ National Research Council suggested that the daily intake of chromium for adults be between 50 and 200 micrograms (1). The chromium levels in the diet of the United States and Western Europe are lower than in the Near and Far East which is at least partly the result of processing (2). Tissue levels are also lower in the United States than in other countries (3, 4).

Inorganic chromium compounds are poorly absorbed in man, amounting to 1-3% regardless of dose or dietary chromium status (5). Organic chromium, such as found in brewer's yeast, is much better absorbed than inorganic chromium (6). Over half of the chromium in brewer's yeast is in a volatile, organic form (7). This form of trivalent chromium, complexed with nicotnic acid and amino acids, is known as glucose tolerance factor (GTF). Among foods, brewer's yeast is the richest source of GTF. This biologically important form of chromium is hypothesized as a co-factor for the binding of insulin to membrane receptors in insulin-sensitive tissues (6).

GTF has been shown to be a requirement for normal carbohydrate metabolism (8). When an animal or human is chromium deficient, the result is an impaired glucose tolerance. To date, there is but indirect evidence to support the view that chromium deficiency occurs in normal human

populations. It does appear that older individuals and those consuming large amounts of carbohydrates might be deficient. Tissue chromium levels have been found to dramatically decrease with age in the United States (2). It has also been shown that chromium is mobilized from body stores as a response to administration of glucose by mouth (9). High consumption of refined sugars and carbohydrates is thus likely to induce chromium deficiencies by excretion. These refined carbohydrates are themselves low in chromium and contribute to the problem.

Diabetics represent the most susceptible group of individuals toward chromium deficiency. Diminished chromium stores have been reported in the hair (10) and liver (11) of diabetic humans. Insulin-requiring diabetics have been shown to have an abnormal rate of chromium absorption. During the first 24 hours after a single oral dose of chromium, these individuals absorb two to four times more chromium than normal subjects (8). Recently, this effect was also seen in diabetic rats given radio-chromium. These rats, when given insulin after chromium, had their chromium levels restored to normal (12). Diabetics have been found to excrete in their urine almost twice as much chromium per day than do normal individuals (13). This is due to the fact that when insulin is taken, 20% of the chromium mobilized from body stores is excreted in the urine. Thus, it appears that administration of insulin may result in an increased excretion of chromium and a tendency to chromium deficiency. This hypothesis is supported by the recent work of Thompson (14) who found insulin-treated diabetics to have significantly lower levels of plasma chromium than normal subjects.

In genetically diabetic mice with hyperglycemia and hyperinsulinemia, GTF administration, both acutely and chronically, reduced the elevated blood glucose levels to normal. Inorganic chromium was completely without effect (7). It was thus hypothesized that diabetic mice had an impaired ability to convert inorganic chromium into the biologically active GTF. If this impairment exists in humans, it may explain the lack of success of chromium supplementation studies such as that by Sherman (15). This group and other groups used inorganic chromium for their studies. For instance, Levine found that the abnormal glucose tolerance of only 4/10 elderly subjects became normal after 1-4 months of inorganic chromium supplementation (16). This improvement of glucose tolerance was not due to retarded glucose absorption or to an increased rise in plasma insulin activity after the glucose load. In fact, in a more recent study, Doisy (8) found that the serum insulin concentration reached lower peak values after a glucose load, following an 8 month chromium supplementation, than before supplementation. This effect was seen in both normal subjects and siblings of diabetics. Thus, it appears that less insulin is required to keep glucose controlled when adequate chromium is present. A study with several offspring of an insulin-requiring diabetic (8) showed that inorganic chromium was ineffective in improving glucose tolerance while a six month supplement of brewer's yeast normalized the glucose tolerance as measured by the glucose tolerance test.

The present study is an attempt to verify the effect of long-term supplementation chromium on glucose control and body lipids in humans using a new high potency chromium yeast.

MATERIALS AND METHODS

Twenty three subjects (ages 17-63) volunteered for the study and their informed consent obtained. Six normal individuals (ages 38-63) served as controls. Five hyperglycemic individuals (ages 47-60) had abnormal blood glucose control as determined by % glycosylated hemoglobin (%GHb) and a high normal fasting blood glucose. Seven individuals (ages 19-62) were insulin-dependent diabetics who had had the disease at least five years. Their insulin requirement was stabilized. Five subjects (ages 39-59) were non insulin-independent diabetics who were taking oral anti-diabetic medication.

With the subjects in a seated position, after an overnight fast, venous blood was collected into a vacutainer containing EDTA. The blood was frozen at -20°C until analysis. The %GHb in the blood was determined with an Isolab kit (Akron, OH) using the optimum room temperature and a control of known value. This column chromatographic method determines the fast hemoglobin HbA_1 which equals HbA_{1a} + HbA_{1a} + HbA_{1c}, with a reproducibility of approximately 5%.

Two other vacutainers of blood were taken. One was used for blood glucose and by a conventional automated enzyme method. The second vacutainer's contents was allowed to clot and the serum frozen until assay. The serum was analyzed for cholesterol and triglycerides by conventional automated methods. High density lipoprotein cholesterol (HDL) was determined after M_n^{++} precipitation by a conventional automated enzymatic method. Low density lipoprotein cholesterol (LDL) was calculated from the formula LDL = Cholesterol = HDL - Triglycerides/5.

Chromium Yeast

The high potency chromium brewer's yeast (Foodform®) is a tan powder containing 2180 micrograms of chromium/g of yeast as assayed by atomic absorption spectroscopy. The % organic chromium, which correlates with biological activity, was determined by the alcoholic extraction procedure of Toepfer and Mertz (17) followed by atomic absorption spectroscopy. The yeast was found to contain 87 ± 6% of organic chromium.

Experimental Design

All the parameters were determined in each subject before supplementation was initiated so that each subject served as his own control. Each subject then took orally each day a gelatin capsule (sugar-free) of 100 milligrams of yeast which contained 218 micrograms of chromium. The %GHb and lipids were determined 2, 4 and 6 months after supplementation began. Statistical comparison within groups was made with the student's test for paired samples by comparison with the pre-dose value.

RESULTS AND DISCUSSION

In this study, the % glycosylated hemoglobin (%GHb) was used to determine the subject's glucose control. The %GHb is much easier to perform than the glucose tolerance test (GTT) and has been found to correlate with the area under the GTT curve (18). The %GHb correlates

with the degree of altered blood glucose control during the previous 1-3 month period (18-20) and decreases when control is improved.

The result of the chromium supplementation on the %GHb of the groups is shown in Table I.

Table I. Effect of Chromium Yeast (Cr) Supplementation on the %GHb of Human Subjects.

Group	% Ghb Before	% GHb 2 Months After Cr	% GHb 4 Months After Cr	% GHb 6 Months After Cr
Normal (n=6)	7.5±1.7	6.6±1.1 N.S.*	6.3±1.0 N.S.	6.6±0.9 N.S.
Hyperglycemic (n=5)	14.6±4.3	6.9±0.7 p<0.005	--	6.3±0.7 p<0.001
Insulin-Dependent Diabetics (n=7)	11.8±2.7	6.6±0.8 p<0.001	7.8±0.4 p<0.005	10.2±2.8 N.S.
Non Insulin-Dependent Diabetics (n=5)	8.8±1.8	7.6±1.2 N.S.	8.9±2.3 N.S.	8.3±2.5 N.S.

*N.S. = Not Significant

There was no significant effect on %GHb for the normal subjects or the Non Insulin-Dependent Diabetics as a result of chromium supplementation. There was a transient improvement after two months for the Insulin-Dependent Diabetics but after six months the %GHb had returned to a value which was lower but not significantly different than the pre-dose level. A study by Rabinowitz (21) corroborates our results with diabetic groups. Rabinowitz, et al., reported a double-blind crossover study of insulin-dependent and non insulin-dependent diabetics supplemented with a brewer's yeast high in GTF (18 μg of chromium/day) and a placebo for 4 months. No improvement in GTT was found in either group of diabetics. However, a recent study by Offenbacher (22) showed that elderly (average age - 78 years) non-insulin dependent diabetics had a 16% lower GTT after 2 months of a daily regimen of 11 μg of chromium in the form of a chromium-rich yeast. The present study also showed a similar improvement (14%) in blood glucose control after 2 months, but after 6 months the blood glucose control was the same as pre-dose levels.

The only group to consistently significantly benefit in the current study was the Hyperglycemics which had average 57% improvement in blood glucose control after 6 months of chromium yeast. Every individual in this group had an improved %GHb after 6 months. The fasting blood glucose for this group declined from 104±17 mg/dl to 92±18 mg/dl although this change was not significant. A significant improvement in GTT was also found by Nordstrom (23) after giving 4 μg of chromium in a brewer's yeast daily for 3 months to hyperglycemic women aged 40-75 years. The

improvement in GTT was 32%, smaller than the present study, but the dose and duration of the supplementation were less than the present study.

A short placebo study was done in order to determine whether the improvement in blood glucose control was due to another factor besides chromium in the yeast. Six individuals, 2 normals, 3 insulin-independent diabetics and 1 non-insulin dependent diabetic, who participated in the original chromium yeast study, were removed from the chromium yeast for 2 months and then supplemented for 2 months with a low-chromium brewer's yeast manufactured using the same process without chromium in the nutrient media. The %GHb before supplementation was 9.9±2.9 and after supplementation was 9.9±3.0. Although the study lasted only 2 months, the previous chromium yeast study showed changes in all groups after 2 months. Thus, it appears that the chromium in the yeast was responsible for the improved blood glucose control.

There were no significant changes in serum cholesterol or triglycerides in any of the groups after 6 months of chromium yeast. There were, as seen with the %GHb data, transient improvements after 2 and 4 months in some groups. For instance, the Hyperglycemic Group had a decrease in cholesterol from 224±13 mg/dl to 186±32 mg/dl after 6 months but the change was not significant. Offenbacher (22) noted a significant decrease in serum cholesterol after 2 months of a chromium yeast but some of this effect was found to be due to a non-chromium component of brewer's yeast. Several other studies (24, 25) also found decreases in serum cholesterol after several months of chromium yeast supplementation but none went as long as this study, 6 months.

The data for high density lipoprotein cholesterol (HDL), which is that fraction of physiological cholesterol considered to be protective (26) against coronary heart disease, is shown in Table II.

Table II. Effect of Chromium Yeast Supplementation on the Serum HDL Levels of Human Subjects

Group	HDL Before CR (mg/dl)	HDL 2 Months After Cr	HDL 4 Months After Cr	HDL 6 Months After Cr
Normal	47±11	64±11 p<0.10	52±14 N.S.	49±17 N.S.
Hyperglycemic	50±9	67±14 p<0.05	--	67±13 p<0.01
Insulin-Dependent Diabetics	52±14	58±11 N.S.	--	59±22 N.S.
Non Insulin-Dependent Diabetics	47±12	47±14 N.S.	48±13 N.S.	--

There were no significant changes in the Normal and Diabetic groups after 6 months. Riales (24) and Elwood (25) observed significant increases in HDL, 12-18% in normals after chromium yeast supplementation

for 6 and 8 weeks, respectively. The present study also shows a slightly significant increase of 36% in the Normal group after 2 months which reverts to pre-dose levels after 6 months.

Table III. Effect of Cr Yeast Supplementation on the Serum LDL of Human Subjects

Group	LDL Before CR (mg/dl)	LDL 2 Months After Cr	LDL 4 Months After Cr	LDL 6 Months After Cr
Normal	161±43	115±37 p<0.1	143±67 N.S.	141±72 N.S.
Hyperglycemic	151±14	109±41 p<0.025	104±54 p<0.1	--
Insulin-Dependent Diabetics	163±73	171±41 N.S.	--	172±79 N.S.
Non Insulin-Dependent Diabetics	152±51	176±32 N.S.	148±90 N.S.	--

The results for the LDL determination are shown above in Table III. LDL is considered to be that protein of cholesterol which carries cholesterol to the cell walls for the deposition that leads to atherosclerosis (27). The only significant change ($p<0.1$) after 4 months was a 31% decline in the LDL of the Hyperglycemic group. The Normal group had a 12% decrease in LDL after 2 months but later it returned to almost pre-chromium levels. Riales (25) in her short chromium yeast supplementation studies also found a significant decrease in LDL. Thus, the Hyperglycemic group appears to have benefited with respect to a LDL lowering as a result of Cr supplementation.

The most significant risk factor with respect to coronary heart disease is the ratio of total cholesterol to HDL (27). The less the ratio, the less the risk of heart disease. The effects of Cr supplementation on this ratio are shown in Table IV.

Table IV. Effect of Cr Yeast Supplementation on the Cholesterol to HDL Ratio (Chol/HDL)

Group	Chol/HDL before Cr	Chol/HDL 2 Months After Cr	Chol/HDL 4 Months After Cr	Chol/HDL 6 Months After Cr
Normal	5.1±0.8	3.1±0.7 p<0.001	4.4±1.6 p<0.1N.S.	5.5±3.3
Hyperglycemic	4.6±0.8	3.0±0.9 p<0.02	2.8±1.0 p<0.01	--
Insulin-Dependent Diabetics	5.2±1.6	3.6±1.1 p<0.1	--	4.9±2.2 N.S.
Non-Insulin-Dependent Diabetics	6.1±2.5	6.3±2.1 N.S.	6.4±2.1 N.S.	--

All groups except the Non Insulin-Dependent Diabetics exhibited significant improvements, i.e., decreases in the Chol/HDL ratio after 2 months of Cr. However, after 4 to 6 months, the only group to maintain a significant change was the Hyperglycemic group which improved by 39%. The study of Riales (24) also showed a slightly significant improvement in the Chol/HDL for normal individuals after 6 weeks of Cr supplementation. The Chol/HDL ratio in the Hyperglycemic Group correlates with an average risk of coronary heart disease before supplementation and a less than 1/2 the average risk after chromium yeast supplementation.

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