Effect of chromium supplementation on chromium status, insulin and glucose level in Non-insulin Dependent Diabetes Mellitus (NIDDM) subjects

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Abstrak

Telah diteliti pengaruh pemberian kromium pikolinat terhadap status kromium tubuh, insulin serum serta glukosa darah pada 20 pasien DMTTI. Subyek dibagi menjadi kelompok perlakuan dan kelompok kontrol masing-masing 10 pasien. Sejumlah 3 pasien gagal menyelesaikan penelitian sehingga jumlah akhir menjadi 17 pasien. Didapatkan nilai median kromium serum 0,09 µg/L dengan rentangan 0,01 - 0,48 µg/L. Tidak didapatkan perbedaan bermakna untuk status kromium tubuh yang dinyatakan sebagai respons relatif kromium, insulin serum maupun glukosa darah antara kedua kelompok setelah pemberian kromium pikolinat 500 µg/hari selama 4 minggu. Data ini menunjukkan bahwa secara statistik belum tampak pengaruh kromium terhadap status kromium tubuh, insulin serum maupun glukosa darah pada pasien DMTTI.

Abstract

The effects of supplemental Cr picolinate on body Cr state, serum insulin and blood sugar in 20 NIDDM subjects was studied. Subjects were divided into a treatment and control group, 10 subjects for each group. Three subjects dropped out of the study. Median value of Cr serum was 0,09 µg/L with a range of 0,01 - 0,48 µg/L. There was no significant difference for the body Cr state expressed as relative chromium response, serum insulin as well as blood sugar between the two groups after supplementation of 500 µg/daily of Cr picolinate for 4 weeks. These datas showed that the effect of Cr supplementation on body Cr state, serum insulin and blood sugar in NIDDM subjects was not statistically significant.

Keywords: glucose metabolism, insulin potentiator, diabetes mellitus control.

Chromium is an essential element in the metabolism of carbohydrate, fat and protein, acting as an insulin potentiator.[1-4] Daily Cr requirement differs according to age. In the adult it varies between 50-200 µg/daily,[5,6] and that amount might not always be present in the daily food consumed. Some factors might affect the biological activity of Cr in food sources i.e. whether it is in the organic or inorganic form, the way food is prepared and menu composition.[7,8,9,10]

The WHO (1996) stated that the normal level of Cr serum is 0,14-0,15 µg/L whereas less than 0,14 µg/L is considered to be Cr deficient.[10] Chromium deficiency in human is still hypothetical although some conditions such as glucose intolerance and increased insulin requirement could be stated as clinical manifestations of the condition.[11]

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In diabetic subjects the Cr serum level is 60% that of the normal subjects.[12] Although there are still differences in results, some studies show the benefit of Cr supplementation in glucose intolerance[13,14] and diabetes.[15,16] The increase of diabetes prevalence after the age of 40[17] and the physiological decrease in body Cr as an individual ages[18] might perhaps be interlinked.

The aim of this study is to determine whether Cr supplementation affects the body Cr state, serum insulin and blood sugar control in NIDDM subjects.

METHODS

Twenty NIDDM subjects, 7 females and 13 males, aged between 40-65 years, with body mass index of 21-25 (females) and 22,5-27 (males), fair and well controlled blood sugar levels[19] participated in the study (Table 1).

After an initial stabilization period of 2 weeks, subjects were randomly divided into treatment and control group. With a single blind study design, the study was

divided into two stages, with a washing period of two weeks in between (Figure 1). The stabilization period was to prepare subjects so that compliance on diet with or without oral hypoglycaemic medicine could be maintained throughout the study.

In the first four weeks (First stage) each subject was given a capsule of Cr picolinate 500 µg/daily or placebo according to their group. After a two-week washing period, another four weeks (Second stage) with the same procedure was done after cross changing the groups.

On weeks 0, 4, 6 and 10 fasting and 1 hour serum Cr, fasting and 2 hours serum insulin, blood sugar level (every 30 minutes for 2 hours) after 75 gram glucose loading were checked.

Cr serum levels were measured with the Neutron Activation Analysis method,[20] serum insulin with the Radio Immunoassay method and blood sugar with the Glucose Oxydase Peroxydase method (Boehringer Mannheim).

Cr status was defined as a relative chromium response which is a ratio of 1 hour Cr level against fasting Cr level[21] and which till now could represent body Cr index.[10]

Table 1. Basic variables characteristics treatment and control group

Variables	Treatment group (n=10) X ± SD	Control group (n=10) X ± SD	
Age (Years)			
Female	56,5 ± 8,3 [4]*	54,7 ± 9,6 [3]*	
Male	52,3 ± 8,0 [6]	49,0 ± 5,0 [7]	
Female + Male	54,0 ± 8,7 [10]	50,7 ± 6,6 [10]	NS
Nutritional Status			
Body Mass Index	26,0 ± 1,8	25,1 ± 1,6	NS
Laboratory			
SGPT	18,1 ± 4,7	18,6 ± 4,2	
Creatinine	0,9 ± 0,1	1,0 ± 0,1	
Albumin	4,5 ± 0,2	4,6 ± 0,2	NS
HbA1C	6,5 ± 0,7	6,7 ± 0,8	NS
Fasting Blood Sugar (Stabilization Period)			
Early phase	116,8 ± 18,5	111,7 ± 13,5	NS
	98,9 ± 33,4	116,5 ± 18,1	NS

Note : NS = Not significant
* = n

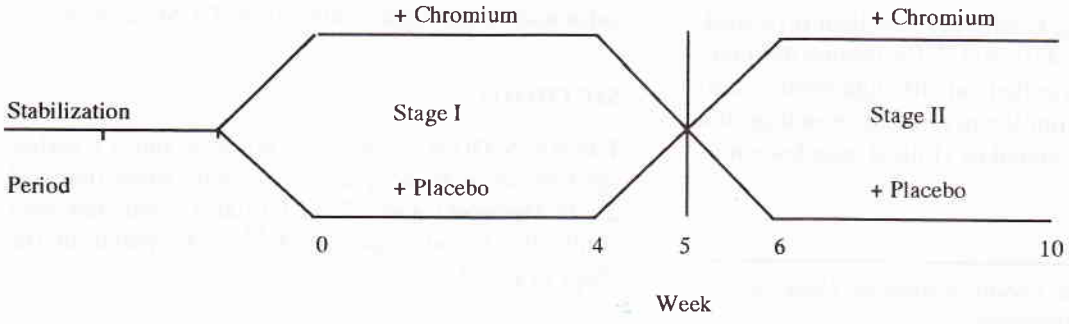

Figure 1. Study design

Blood sugar control was expressed as "Δ area under the curve" which was the difference between area under the curve and fasting blood sugar area.

Diet stabilization compliance was established through quantitative food review at week 0 and 6 with the "two days recall" method, helped by using food models from the Nutrition Study and Development Centre, Bogor, Indonesia and a subsequent analysis with Indonap 2.0[21] was used.

Statistical analysis was done at stage I, stage II and both stage I and II. Mean value and student T test were used for normal distribution, where as median value, Wilcoxon and Mann Whitney tests were used for abnormal distribution.

RESULTS

Chromium serum level for all subjects was 0,09 μg/L with a range of 0.01-0.48 μg/L. There was no significant difference for the relative chromium response between the treated and control group in stage I and stage II.

Fasting and 2 hours serum insulin levels showed an increase for both groups (Table 2) followed directly by a decrease in stage II (Table 3) and with an increase again at stage I and II (Table 4). All the differences were not statistically significant.

Table 2. Effects of supplemental chromium on serum insulin and blood sugar at stage I

Variables	Before subjects extraction		After subjects extraction	
	Treatment group (n = 10) P	Control group (n = 10) P	Treatment group Hypochrom (n = 7) P	Control group Hypochrom (n = 5) P
Insulin (μU/mL)	Median (Range)	Median (Range)	Median (Range)	Median (Range)
Fasting:				
week 0	12,6 (4,4 - 22,1)	9,1 (7,5 - 21,0) NS‡	11,3 (4,4 - 22,1)	9,0 (7,8 - 16,7) NS‡
week 4	16,9 (7,1 - 28,7) NS§	13,1 (8,4 - 21,4) NS‡ NS§	17,7 (7,1 - 28,7) NS§	16,4 (10,0 - 21,4) NS‡ NS§
2 hours:				
week 0	46,0 (36,3-161,3)	55,6 (23,9-143,0) NS‡	48,4 (36,3-161,3)	78,5 (46,3-143,0) NS‡
week 4	55,9 (27,6-136,6) NS§	69,5 (27,7-248,5) NS‡ NS§	58,9 (27,6-136,6) NS§	76,2 (50,4-248,5) NS‡ NS§
Glucose (mg/dL.second)	X ± SD	X ± SD	X ± SD	X ± SD
Δ week 0	18433,5 ± 3814,4	16470,7 ± 3225,5 NS*	19338,8 ± 2045,9	17385 ± 1926,5 NS*
week 4	16396,5 ± 3293,2 NS†	15867,0 ± 4838,8 NS* NS†	16913,6 ± 3392,9 NS†	16161 ± 1359,1 NS* NS†

Note: NS : Not Significant (p > 0,05), * : Independent t test, † : Dependent t test, ‡ : Mann Whitney test, § : Wilcoxon test

Table 3. Effects of supplemental chromium on serum insulin and blood sugar at stage II

Variables	Before subjects extraction		After subjects extraction	
	Treatment group (n = 8) P	Control group (n = 9) P	Treatment group Hypochrom (n = 5) P	Control group Hypochrom (n = 7) P
Insulin (μU/mL)	Median (Range)	Median (Range)	Median (Range)	Median (Range)
Fasting :				
week 6	9,7 (6,9 - 13,4)	12,5 (6,6 - 23,6) NS‡	8,8 (6,9 - 10,3)	12,3 (6,6 - 20,3) NS‡
week 10	10,2 (8,0 - 21,5) NS§	11,2 (7,6 - 24,1) NS‡ NS§	9,6 (8,0 - 21,5) NS§	11,4 (9,5 - 24,1) NS‡ NS§
2 hours:				
week 6	78,6 (27,4-223,3)	67,2 (33,4-182,8) NS‡	76,1 (56,8-223,3)	45,1 (33,4-162,0) NS‡
week 10	69,4 (34,0-117,5) NS§	62,3 (32,3-240,3) NS‡ NS§	71,1 (37,4- 99,8) NS§	63,3 (32,3-240,3) NS‡ NS§
Glucose (mg/dL.second)	X ± SD	X ± SD	X ± SD	X ± SD
Δ week 6	14170,6 ± 4133,8	17000,0 ± 2702,5 NS*	13593 ± 4645,7	16671,4 ± 2880,4 NS*
week 10	15690,0 ± 4907,5 NS†	18258,3 ± 2644,1 NS* NS†	16215 ± 5792,6 NS†	18117,8 ± 2589,6 NS* NS†

Note: NS : Not Significant (p > 0,05), * : Independent t test, † : Dependent t test, ‡ : Mann Whitney test, § : Wilcoxon test

Table 4. Effects of supplemental chromium on serum insulin and blood sugar at stage I and II

Variables	Before subjects extraction		After subjects extraction	
	Treatment group (n = 18) P	Control group (n = 19) P	Treatment group Hypochrom (n =12) P	Control group Hypochrom (n = 12) P
Insulin (μU/mL) Fasting :	Median (Range)	Median (Range)	Median (Range)	Median (Range)
week 0,6	10,25 (4,4 - 22,1)	9,5 (6,6 - 23,6) NS‡	9,55 (4,4 - 22,1)	11,8 (6,6 - 20,3) NS‡
week 4,10	13,2 (7,1 - 28,7) NS§	11,4 (7,6 - 24,1) NS‡ NS§	10,0 (7,1 - 28,7) NS§	12,9 (9,5 - 24,1) NS‡ NS§
2 hours:				
week 0,6	58,6 (27,4-223,3)	56,4 (23,9-182,8) NS‡	62,3 (36,3-223,3)	61,0 (3349-162,0) NS‡
week4,10	61,9 (27,6-136,6) NS§	64,3 (27,7-248,5) NS‡ NS§	66,3 (27,6-136,6) NS§	70,1 (32,3-248,5) NS‡ NS§
Glucose (mg/dL.second)	X ± SD	X ± SD	X ± SD	X ± SD
Δ week 6	16583,3 ± 4389,7	16760,5 ± 2978,9 NS*	16988,7 ± 4417,5	16968,7 ± 2485,7 NS*
week 4,10	16713,3 ± 4265,2 NS†	16999,7 ± 4039,7 NS* NS†	16622,5 ± 4313,9 NS†	17302,5 ± 2311,9 NS* NS†

Note: NS : Not Significant (p > 0,05), * : Independent t test, † : Dependent t test, ‡ : Mann Whitney test, § : Wilcoxon test

Some investigators reported that suplemental Cr was more beneficial in NIDDM subjects with low level of body Cr.[23,24] With a cut off point of 0.14 μg/L Cr serum (WHO, 1996), an extraction of hypochromic subjects (<0,14 μg/L Cr serum) was done in this study to see whether it gave the same results. Statistical analysis on hypochromic subjects from the treatment and control group showed no significant differences (Table 2,3,4).

The same results were seen for blood sugar levels. With regard to blood sugar control, there was no significant difference between the treatment and control group at stage I (Table 2) and stage II (Tabel 3) even when the hypochromic subjects were extracted.
Overall analysis for both stage I and II showed a different outcome. Increase in the Δ area under the curve which was seen in both groups was directly followed by a decrease in the hypochromic subjects from the treatment group and an increase in the hypochromic subjects of the control, even though this was still not statistically significant. Above datas showed that 500 μg Cr picolinate daily as a supplementation for 4 weeks in NIDDM subjects did not control serum insulin and blood sugar better than without.

DISCUSSION

Body Chromium

Serum Cr levels in this study showed the same results in NIDDM patients as reported by Morris which was 60% of the normal subjects.[12] In this study, the effect of Cr supplementation on relative chromium response was not seen in the treatment group as well as control. The very low serum Cr levels and the still not clearly known Cr metabolism made this fact difficult to explain. This might be linked to the fact that there was still a very small number of studies done on hyperglycemic and diabetic subjects in connection with body Cr levels.

Serum Insulin

Improvement in insulin levels which was statistically significant was reported by Anderson using 500 g Cr picolinate twice daily for 2 - 4 months in 60 NIDDM subjects.[24]

In this study the change in serum insulin level 2 hours after glucose loading was inconsistent although overall it has been shown to be beneficial to the treatment group. In stage I (Table 2) both groups showed an increase in serum insulin i.e., the control group: 25% and the treatment group: 21%, whereas in stage II (Table 3) decrease of serum insulin in the treatment group (11%) was bigger than control (7%). The combined analysis of both stage I and II (Table 4) showed that the increase in the control group (14%) was bigger than the treatment group (5%). Nevertheless, all the findings were not statistically significant. It seems that the dosage of Cr, length of treatment and the number of subject made these results different from Anderson's study.

Blood Glucose

Improvement in glucose tolerance was first reported by Glinsmann and Mertz in 3 out of 6 NIDDM subjects who were given 180-1000 g Cr chloride for 15-120

days.[15] Some results was found by Levine in 4 out of 10 diabetic subjects given 150 µg/daily for 4 months.[25] On the other hand, other investigators reported no improvement in blood glucose after Cr supplementation.[26,27]

In this study the blood sugar control showed inconsistent result. Decrease in stage I (Table 2) was followed by an increase in stage II (Table 3). This might be connected in some way to the individual variety of the subjects especially with regard to their diet. The quantity of food intake between the treatment group in stage I which became the control group in stage II showed an increase of carbohydrate intake (20%) although these findings were not statistically significant.
Analysis on both stage I and II which earlier showed an increase in the "Δ area under the curve" in both groups, after extraction was soon followed by a decrease in the hypochromic treatment subjects and an increase in the hypochromic control subjects (Table 4). It seems that Cr supplementation was more beneficial to the diabetic subjects with low serum Cr levels although this was not statistically significant.

CONCLUSION

After statistical analysis, findings in this study showed that supplemental Cr picolinate 500 µg/daily for 4 weeks in NIDDM subjects does affect serum insulin levels and blood sugar control.

A bigger number of subjects with a longer period of treatment, using larger doses of Cr (800-1000 µg/daily) might be needed to determine this matter further.

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