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Original Article

Magnesium intake and insulin resistance in obese adolescent girls

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Abstract

Background The worldwide increase in the prevalence of cardiovascular diseases in adulthood is related to obesity in children and adolescents. Insulin resistance and hyperinsulinemia observed in obese individuals are the precursors of cardiovascular diseases and type 2 diabetes mellitus. Magnesium, through its action on insulin receptors, is proposed to be an important factor in preventing insulin resistance.

Objective The aim of this study was to assess the association between magnesium intake and insulin resistance in obese adolescent girls.

Methods This was a cross-sectional study on obese adolescent girls in Yogyakarta, Indonesia. Insulin resistance was defined as a HOMA-IR index of 3.16 or more. HOMA-IR was calculated using fasting insulin and plasma glucose levels. Magnesium intake and energy adjusted magnesium intake were measured using a 24-hour food recall method on 6 non-consecutive days.

Results Of 78 obese adolescent girls included in our study, 56% of them were found to be insulin resistant. Magnesium intake was only 61% of the recommended daily requirement for adolescent girls. There were no significant associations between magnesium intake and either HOMA-IR or hyperinsulinemia.

Conclusion Our study does not find an association between insulin resistance and magnesium intake in obese adolescent girls. **[Paediatr Indones. 2009;49:200-4]**.

Keywords: *magnesium intake, insulin resistance, obesity, female, adolescent*

Recent epidemiological studies have clearly shown that increasing rates of cardiovascular disease in adulthood is related to obesity in children and adolescents.[1,2] Insulin resistance and hyperinsulinemia observed in obese individuals are the precursors of cardiovascular diseases and type 2 diabetes. Recently, an epidemiological study in the United States showed that 52.1% of obese adolescents were insulin resistant.[3] Since the prevalence of childhood obesity in developing countries has also been rising,[4] studies looking at the role of environmental factors in the development of insulin resistance are urgently required.

Although the role of macronutrient intake and obesity in the development of type 2 diabetes mellitus has been well established, the role of micronutrient intake is still poorly understood. Magnesium intake has been shown to be related to insulin resistance in

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adulthood.[5,6] Magnesium supplementation in type 2 diabetes mellitus patients has also been shown to increase insulin sensitivity.[7] Magnesium deficiency is believed to influence the hormonal activity of insulin in cells.[8] At the insulin receptor level, hypomagnesemia reduces tyrosine kinase activity and autophosphorylation.[8] Both of these processes lead to a decrease in sensitivity to insulin.[9-12]

In a small cross sectional study, Huerta *et al*[13] observed the relationship between magnesium intake and insulin resistance in childhood. Energy-adjusted magnesium intake was inversely related to the homeostasis model assessment (HOMA) value and the fasting insulin level. This finding is very important because it may give a mean to help preventing the development of insulin resistance. Therefore, we need to further evaluate the role of magnesium intake in the development of insulin resistance in an independent population. The aim of this study was to assess the association between magnesium intake and insulin resistance in obese adolescent girls in Yogyakarta, Indonesia.

Methods

We invited 78 obese adolescent girls to participate in this cross sectional study. The minimum sample size estimated for this study was 72, assuming 25% prevalence of insulin resistance, 0.1 precision and a 95% confidence interval.[14] Subjects were selected from a previous obesity screening program carried out in six junior high schools in Yogyakarta, Indonesia.

Obesity was defined as BMI (body mass index) at or above the 95th percentile of the Center for Disease Control (WHO-CDC) 2000 growth reference standard.[15] BMI was calculated by dividing in weight in kilograms (kg) by the square of height in meters (m^2). Weight was measured using an electronic digital scale with an accuracy of 0.1 kg. Height was measured using a microtoise with 0.1 cm accuracy. Both instruments were calibrated by the Department of Metrology, Yogyakarta.

Ethical clearance was obtained from Ethical Commission of Medical and Health Research, Medical School, Gadjah Mada University, Yogyakarta. Written informed consents were obtained from the subject's parents before the data were collected.

Insulin resistance

The homeostasis model assessment for insulin resistance (HOMA-IR) was used as a proxy for insulin resistance. HOMA-IR was calculated from the fasting plasma glucose level and insulin concentration using the following formula: HOMA-IR = (fasting insulin[mg/dL] x fasting glucose [mU/mL])/405.[16]

Blood samples for analysis were collected from subjects after a minimum of 8 hours fasting. Fasting plasma glucose was measured with a hexokinase reagent kit (DiaSys, Germany) according to the manufacturer's instructions. The plasma glucose assay was run in duplicate, assuming that the intra-assay coefficient of variation (CV) was less than 3%. Fasting insulin concentration was measured using the ELISA (enzyme-linked immunosorbent *assay)* method (Elecsys, USA).

Assessment of magnesium intake

The mean dietary energy and nutrient intake was obtained by conducting 24-hour food recalls on six non-consecutive days. The number of days required to estimate magnesium intake was based on Beaton's equation[17] with 1.96 for $Z\alpha$ (95% Confidence Interval), 35% for coefficient of variance and 30% for tolerance value. Total daily unadjusted magnesium intake was determined. Energy–adjusted magnesium intake was calculated by dividing the total daily unadjusted magnesium intake by the daily energy intake.

Other measurements

We measured waist circumference (the shortest distance around the area below the rib cage and above the umbilicus)[18] using a non-stretchable tape measure. Since the intake of dietary fiber,[19] fat, calcium and phosphorous[20] is known to influence magnesium absorption in humans, we also measured the intake of these nutrients.

Statistical analysis

We used the t test and the Mann-Whitney test to analyze the difference between the insulin resistance group and the non-insulin resistance group. Pearson correlation and Spearman correlation were used to determine the relationship between magnesium intake and markers of insulin resistance.

Results

Dietary magnesium

Intake of magnesium, calcium and phosphorous was below the recommended dietary allowance (RDA) for Indonesian adolescent girls. Magnesium intake was only 61.3% of the RDA while intakes calcium and phosphorous were only 21.1% and 52.3% of the RDA, respectively.

Magnesium absorption can be influenced by other nutrients such as dietary fiber, fat, calcium, and phosphorous. Higher magnesium intake was associated with higher intake of several other nutrients e.g. fiber (r=0.52, P<0.001), calcium (r=0.57, P<0.001) and phosphorous (r= 0.29, P=0.01). In this study, dietary fat intake was not related to higher magnesium intake (r=0.12, P=0.31).

Markers of insulin resistance

The prevalence of insulin resistance in obese adolescent girls in this study was 55.7% (44 out of 78). The median (Q1;Q3) HOMA-IR index value was 3.30 (2.49;4.27), and the range of HOMA-IR values was from 0.91 to 25.78.

The means (SD) fasting plasma glucose and fasting insulin levels were 88.1(17.9) mg/dL and 17.7(10.9) mU/mL, respectively.

Subjects with insulin resistance (IR) have a greater mean BMI than subjects without insulin resistance (**Table 1**). Fasting insulin concentration was associated with insulin resistance (P<0.001) while fasting plasma glucose level was not associated with insulin resistance (P=0.13) **(Table 1).**

Table 1. Characteristics of subjects with and without insulin resistance

Characteristics	Insulin resistant	Non-insulin resistant	P
Mean (SD) age (year)	13.80 (0.85)	13.47 (1.00)	0.12
Mean (SD) weight (kg)	73.11 (8.16)	66.75 (7.52)	0.01
Mean (SD) body mass index (kg/m^2)	30.49 (2.54)	28.54 (2.17)	0.01
Median (Q_1; Q_3) waist circumferrence (cm)	89.50 (85.63; 96.00)	86.00 (83.00; 89.00)	0.01
Median (Q_1; Q_3) fasting insulin concentration (mU/mL)	19.17 (16.29; 23.95)	11.16 (8.88; 13.92)	<0.001
Median (Q_1; Q_3) fasting plasma glucose concentration (mg/dL)	87.00 (79.25; 96.00)	84.00 (77.25; 90.25)	0.13
Nutrient intakes			
Mean (SD) energy (kcal)	1169.28 (362.90)	1119.40 (256.59)	0.48
Mean (SD) fiber (g)	5.95 (2.27)	6.29 (2.51)	0.63
Mean (SD) phosphorous (mg)	495.02 (177.84)	545.22 (425.32)	0.44
Median (Q_1; Q_3) calcium (mg)	183.43 (130.86; 269.40)	166.19 (124.73; 267.47)	0.75
Median (Q_1; Q_3) magnesium (mg)	136.50 (109.33; 166.99)	120.15 (98.83; 165.44)	0.22
Median (Q_1; Q_3) energy-adjusted magnesium intake (mg/kcal)	0.12 (0.10; 0.14)	0.10 (0.09; 0.13)	0.17

Median (Q_1; Q_3) was used to present estimation and dispersion of data when the data were not normally distributed.

Table 2. Markers of insulin resistance in total magnesium intake quartiles (g/day)

Total magnesium intake / Markers of insulin resistance	Q1 (n=19) 35.23-106.60	Q2 (n=20) >106.60-129.00	Q3 (n=20) >129.00-166.01	Q4 (n=19) >166.01-466.80	P
Mean (SD) fasting plasma glucose (mg/dL)	94.21(28.87)	86.70(12.84)	86.05(12.34)	86.32(13.04)	0.44
Mean (SD) fasting insulin (mU/mL)	14.21(4.60)	18.28(8.86)	19.09(11.79)	19.19(15.82)	0.46
Mean (SD) HOMA-IR	3.35(1.72)	3.96(2.26)	4.03(2.67)	4.48(5.33)	0.77

Table 3. Markers of insulin resistance in energy-adjusted magnesium intake quartiles (g/kcal/day)

Energy-adjusted magnesium intake / Markers of insulin resistance	Q1 (n=19) 0.05-0.09	Q2 (n=20) >0.09-0.11	Q3 (n=20) >0.11-0.13	Q4 (n=19) >0.13-0.42	P
Mean (SD) fasting plasma glucose (mg/dL)	91.79(28.99)	86.45(12.59)	85.45(11.99)	89.63(14.16)	0.68
Mean (SD) fasting insulin (mU/mL)	14.68(6.31)	18.22(8.12)	19.24(11.58)	18.63(15.96)	0.58
Mean (SD) HOMA-IR	3.34(1.85)	3.97(2.20)	4.12(2.71)	4.38(5.30)	0.79

Magnesium and insulin resistance

Total magnesium intake and energy-adjusted magnesium intake were not different between the insulin resistant and the non-insulin resistant groups **(Table 1)**. Using one-way ANOVA analysis, we found no relationship between total magnesium intake and markers of insulin resistance **(Table 2)**. This relationship was not statistically significant even after adjustment of total magnesium intake for daily energy intake **(Table 3)**.

Discussion

The role of magnesium in the development of insulin resistance is not yet clearly understood. As an essential micronutrient, magnesium has roles in more than 300 metabolic reactions.[21] Magnesium is a part of Mg-ATP complex which is known to be an important mediator for energy production. Magnesium controls blood glucose concentration by increasing glycolytic process in the erythrocytes.[21] Several studies have shown that magnesium deficiency is associated with increased intracellular calcium levels and increased membrane microviscosity, which impair insulin-receptor interaction.[22]

Using six-day food recalls we observed that the mean magnesium intake of our subjects was below the RDA for Indonesian adolescent girls (61.3% RDA). The mean (SD) energy-adjusted magnesium intake in our study was 0.12 (0.05) mg/Kcal. This finding was similar to that of Huerta *et al*[13] who also found that energy-adjusted magnesium intake in obese adolescents was 0.12 (0.004) mg/Kcal.

The first study to explore the relationship between magnesium intake and insulin resistance in adolescents was conducted by Huerta *et al*,[13] using a cross sectional study in obese and non-obese adolescents. No significant relationship between total magnesium intake and insulin resistance was found, but after adjusting magnesium intake for energy intake, this relationship became significant.[13] This finding indicated that individual variation in food intake influences the relationship between magnesium intake and insulin resistance.

We used HOMA-IR to determine the occurrence of insulin resistance in obese adolescent girls. Our study, however, did not find the same association between insulin resistance and either magnesium intake or energy adjusted magnesium intake in adolescents. There were some differences between our study and that of Huerta *et al.*[13] For example, we only recruited obese adolescent girls while Huerta *et al*[13] recruited adolescents of both sexes with various body mass indexes, races and ages. Studies in adulthood observed that magnesium intake was related to insulin resistance[5,6] and its supplementation was related to the improvement of insulin sensitivity.[7]

Several factors may confound the relationship between magnesium intake and insulin resistance. Lee *et al*[3] found that age, BMI, and waist circumference were related to insulin resistance in adolescents. After adjustment for age, BMI, and waist circumference, we found that magnesium intake was not related to the markers of insulin resistance. Increased magnesium intake was not correlated with decreased fasting blood glucose level ($r=-0.18$), fasting insulin concentration ($r=-0.004$) and HOMA index ($r=-0.06$).

There were several limitations to our study. Because we used 24-hour food recall, under- or over-reporting in our data collection may have occurred. Under-reporting that varies with sex, age, BMI, and educational level may influence the interpretation of the relationship between diet and diseases.[23] We were also well aware that our results could not be generalized into all populations since our subjects were limited to obese adolescent girls. Another study with different types of subjects is needed for further investigation into the relationship between insulin resistance and magnesium intake.

In conclusion, our study observes no association between insulin resistance and magnesium intake in obese adolescent girls. We also find that magnesium intake in obese adolescent girls is lower than recommendation for adolescent girls. Another study with a larger sample size, different dietary assessment and additional measurements of magnesium status (e.g. intracellular magnesium level or blood free magnesium level) is highly recommended.

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