Hypomagnesemia has been associated with increased insulin resistance. It is thought that with the down regulation of magnesium-dependent mechanisms to take up glucose into cells, cells become increasingly insulin resistant. In a longitudinal study following 5000 American young adults for 20 years, they found that high magnesium diets were significantly correlated with the decrease of diabetes incidence compared to low magnesium diets. A double-blind, random, placebo-controlled trial found that a 6 month MgCl₂ supplement significantly increased insulin sensitivity compared to a placebo supplement. Another study found that this not only applies to adults but to children: obese children who ate low magnesium diets had higher insulin resistance than their lean peers who ate high magnesium diets. As the evidence builds to support the role of magnesium in glucose uptake and insulin sensitivity, it is still undecided whether magnesium supplements are as good as eating high magnesium diets. I propose a study designed to test which is more beneficial: magnesium supplements or high magnesium diets. The study will show whether or not magnesium supplements are as good as high magnesium diets in decreasing insulin resistance.

Key words: Magnesium, hypomagnesemia, insulin resistance, diabetes, pre-diabetes,
According to the 2005-2006 NHANES study, almost half of Americans (48%) do not get the recommended amount of magnesium in their diets. This has increased from 44% who did not get adequate magnesium in the 2001-2002 NHANES study. The rate of type 2 diabetes incidence has increased during this time. It is hypothesized that low magnesium consumption is one process by which one becomes insulin resistant and eventually diabetic (1).

Magnesium deficiency has gained more attention in the past couple of years. Both dietary magnesium levels and serum magnesium levels have been related to incidence of type 2 diabetes (1). One of the mechanisms suggested for this association has been the link between magnesium and insulin. Magnesium seems to be involved in a post-receptor mechanism for relaying the signal from insulin to the cell to take up glucose (2). It is thought that the down regulation of magnesium-dependent mechanisms for glucose uptake causes cells to become increasingly insulin resistant, which leads to type 2 diabetes.

A longitudinal study followed about 5000 Americans ages 18-30 for 20 years to see if magnesium intake had an impact on the incidence of diabetes. They examined the subjects at baseline and for six follow-up visits, only including patients who did not initially have diabetes. They measured the dietary magnesium intake using a validated interviewer-administered CARDIA Diet History Questionnaire. They also measured fasting plasma glucose, plasma insulin, glucose tolerance, and inflammatory markers. When analyzing the data, they found that the rate of diabetes incidence was 47% lower for the quintile with the highest magnesium intake than for the lowest quintile. They concluded that total dietary magnesium intake was inversely related to the incidence of diabetes (3).

While the first study found that increased dietary magnesium decreased the incidence of diabetes, the question remains: Does magnesium supplements have the same effect? Another
study took 52 individuals who had decreased insulin sensitivity (fasting venous plasma glucose level of ≤6.94 mmol/l) and performed a double-blind, randomized, placebo-controlled trial to test whether a magnesium supplement would decrease fasting blood glucose levels in individuals with hypomagnesemia. The subjects took the magnesium supplement or placebo for six months. At the end of six months, they tested fasting blood glucose, fasting serum insulin, and other markers for insulin resistance. In the supplement group, the fasting blood glucose was significantly lower and the fasting serum insulin level was decreased, but not significantly. The other insulin resistance markers showed a favorable relationship between magnesium supplementation and decreased insulin resistance. This study supports the idea that magnesium supplementation will decrease blood glucose and insulin resistance markers in type 2 diabetes (4). However, only subjects with hypomagnesemia were included in their study.

Another study researched the effect of magnesium intake on children. They studied 24 obese nondiabetic and 24 lean children, measuring their magnesium intake and serum magnesium levels. Serum magnesium and magnesium intake were inversely related with fasting insulin, indicating that those children who ate less dietary magnesium had greater insulin resistance than their peers. They suggested that the decreased serum magnesium was because of the decreased dietary magnesium, which supports the findings that serum magnesium is associated with insulin resistance, even in children (5). While this study was small, it adds to the evidence suggesting that low magnesium intake is associated with insulin resistance.

While the evidence builds supporting the idea that magnesium intake is inversely associated with insulin resistance, it is not clear that dietary magnesium and magnesium supplements are equal in their effects. As one study pointed out, magnesium rich foods are components of a healthy diet (3). This may be a confounding factor in determining the effects of
magnesium on insulin sensitivity. However, a second study found that magnesium supplements can help decrease insulin resistance (4).

With regards to insulin sensitivity and diabetes prevention, is it as beneficial to take a magnesium supplement as it is to eat magnesium rich foods? As a null hypothesis, I will state that neither increased dietary magnesium nor a magnesium supplement will decrease insulin resistance or diabetes incidence. However, I do expect both to have an impact, with dietary magnesium having the greatest impact.

I will advertise a free blood glucose screening for participating in a study, and will measure participants’ fasting blood glucose. At the screening, we will also take the participants’ height, weight, blood insulin levels, and serum magnesium levels. As the participants are tested, I will set apart the ones who qualify for the study. Those who qualify must be obese (BMI>30), be age 25-65 years old, and have a fasting blood glucose of 100-125 mg/dl. I will randomly assign one third of the participants to each group: MgCl2 supplement pills, high magnesium diet, and placebo pill. I will instruct the participants with the supplement and the placebo to take one each day. Food will be provided for those on a high magnesium diet once per day, with instruction to eat high magnesium foods at other times.

I will continue the study until I have 1000 participants. At the end of 6 months, I will invite the participants back to test their fasting blood glucose, blood insulin levels, and serum magnesium levels. I will also use the CARDIA Diet History Questionnaire to ask participants their dietary magnesium intake. I anticipate that both those on the supplement and the dietary magnesium will have better blood markers, with the dietary magnesium showing the most improvement. This will indicate that magnesium supplements improve insulin sensitivity, but magnesium containing foods help even more.
REFERENCES


1st reviewer:

- This makes it sound like high magnesium diets had a positive correlation with insulin resistance.
  - I fixed the sentence to be more clear
- It seems like it would make more sense to make this your introductory paragraph. Then you could move into the proposed mechanism for the relationship between insulin resistance and diabetes (what you wrote in your first paragraph). That might transition better into discussing the papers you address.
  - I switched the paragraphs.
- What kind of dietary assessment? Was it validated?
  - I included the information: validated interviewer-administered CARDIA Diet History Questionnaire.
- How many?
  - I included the number 52.
- Is this the expected result or not? Is the explanation that less insulin is needed for these people because they have more of a response to insulin? Since it kind of confused me, I would either explain a little more or not include it at all because it is not statistically significant.
  - I thought it was pretty clear, but I changed the word order a little to help it be clearer.
- Are there other lifestyle modifications besides consuming more Mg?
  - I deleted the confusing sentence, because it didn’t add to my paper.
- Explain this comment more to finish it off. You could simply say that it might be other proponents of the healthy diet that have the effect on insulin.
  - I changed the sentence slightly to include that idea.
- On all of the journals that are consecutively numbered (meaning that volume 2 starts at page 300, for instance), you don’t need to put the issue number in parentheses.
  - But, it is consistent, which follows the instructions.
- Does Diabetes need to be spelled out or does it have an abbreviation like most words used for journals?
  - That’s what it’s supposed to be.
- Making the title a little bit more descriptive would be helpful. For instance, you could tell the direction of the relationship (are they inversely related? Positively correlated?) between magnesium deficiency and insulin resistance.
  - Good suggestion. I adjusted the title.
- Another point related to your research design is to consider using a placebo for the normal diet. That would at least blind two of the groups.
  - Good idea. I made the change.
- Furthermore, you might consider a way to track how much Mg the participants are actually consuming—those in the high Mg diet group as well as those in the other groups. Otherwise, you won’t really know how much Mg they are consuming. Keeping a food log would make the study much more demanding, but it is something to consider.

Second reviewer:

- Format -probably want to put a few spaces between the title and the assignment information
Done

• Awkward phrasing/transition. Maybe use a colon: “children: obese children who ate low magnesium...”
  o Fixed

• Avoid “I”/”we” and “you”. Also, is the proposal for a new study supposed to be integrated into the main paper or separate? I thought they were separate, but now that I look at the directions I'm not sure.
  o I don’t know. I will keep it included unless the TA tells me to take it out.

• Unclear sentence. Did more or fewer Americans have inadequate magnesium intake in 2001-2002?
  o I fixed the sentence.

• “uptake” is a noun, “take up” or “absorb” are verbs
  o Ok. I fixed the ones indicated.

• Sentence sounds redundant – be more specific, and maybe combine this with the next sentence
  o I added more information from the last reviewer, so it sounds better.

• These don't seem to be contradictory studies
  o I reworded the sentence to make my point of the differences clearer.

• The topic is interesting and the studies all connect well. You have enough references but you may need to discuss four studies in detail instead of using two for background and three for discussion; however, I'm not sure about this so you should ask a TA.
  o In class, Dr. Parker said that it is fine to have a short sentence for one and go into detail for the others.

• A concluding paragraph would be helpful to clearly tie the three studies together before moving on to the study proposal. Paragraph #1 on page #4 could be split into one conclusion and one introduction to the proposal.
  o Good idea. I made it fit.

• Good job sticking to the page limits. Making the proposal more concise would allow more room for a conclusion without going over the page limit. I think the proposal is supposed to be separate from the discussion and doesn't need to be mentioned in the abstract but I could be wrong.
  o I tried to fix it as best I can.

• Page 2, paragraph 1, last sentence: explain how gestational diabetes connects to the rest of the paper.
  o I actually just took that out. That is something for another discussion.

• Page 3, paragraph 1, last three lines: Did the study really say anything about lifestyle modification? The beginning of the paragraph only mentioned a placebo, not lifestyle modification. Also, the last sentence could flow better with the rest of the paragraph.
  o The study stated that as a side note, looking at other studies done. However, I took the information out to help with clarity.

TA Review:

• I put my name on the top like the TA said to.
• Make sure you only have a few sentences of background/introduction and then give a few sentences about the specific studies you reviewed in-depth. Also, include a sentence or two about your proposed study and your hypothesis of the expected outcome. Cap it all off with a conclusion or summary statement. These are the specifics Dr. Parker is looking for in the abstract.

  o I made a couple of adjustments, but feel like it was already pretty close to what they asked. Mostly I added a concluding statement.

• Also, review all of the instructions to make sure that your paper fits the assignment. I want you to read it aloud and make any needed changes before you submit it. Also, watch your in-text citations – they should have the (#) before the period of the sentence.

  o I changed the in-text citations and went through the paper with the instructions one more time. (Even though this is a cop out comment.)

• Other than that, your paper looks good!