Exploring alternative approaches to diabetes

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Many patients with diabetes mellitus use complementary and alternative medicine (CAM) to help manage their condition.[1] Like any pharmacological or surgical intervention, CAM treatments have their place in disease management. However, it is imperative that patients and clinicians alike have a thorough understanding of these therapies prior to adding them to standard care.

Unfortunately, most patients do not tell their physicians when they are taking CAM treatments because they fear being embarrassed or censured.[2] Keeping this information from physicians can lead to unnecessary confusion and complications. Open and nonjudgmental communication is necessary if both physicians and patients are to avoid the pitfalls of CAM treatments and instead benefit from including some of these treatments in a medical regime.

The evidence for the uses of CAM treatments in patients with diabetes is extensive. In this article, we will look at some of the more commonly used treatments.

Cinnamon

Cinnamon has long been used in the treatment of patients with type 2 diabetes mellitus (T2DM). Several studies have found the spice to be effective in reducing fasting blood glucose (FBG).[3] In addition, some studies have shown improvements in lipid profiles and other parameters of metabolic syndrome, such as systolic blood pressure and body composition.[4,5]

However, not all the studies have shown such positive results. In fact, a meta-analysis published in *Diabetes Care* in January 2008 showed no significant improvement in HbA1c, FBG, or lipid parameters in patients taking cinnamon.[6]

Regardless, cinnamon is generally recognized as safe. Under the guidance of physicians, cinnamon can be added to a treatment regimen at a dosage of one-half teaspoon daily.

Chromium picolinate:

Chromium picolinate (CrPic) has been used in the treatment of patients with T2DM for its reported hypoglycemic effect. Studies have found that CrPic improves insulin sensitivity and glucose control, as well as attenuates weight gain and visceral fat accumulation.[7] In addition, some research has found that chromium supplementation reduces HbA1c levels and improves lipid profiles.[8]

However, not all studies are supportive, with some studies showing minimal or no effect.[9] The inconsistent data regarding chromium supplementation appear to be due, at least partially, to other differences in patients. Patients who are hyperinsulinemic or obese have a much more pronounced and predictable response to chromium supplementation than those who are not.[9,10]

If patients and their physicians agree to initiate treatment, beginning with 200 mcg per day is considered reasonable and safe. Higher dosages may be associated with side effects, such as kidney and liver problems.[11]

Magnesium

Magnesium supplementation is critically important for patients with T2DM. Magnesium plays an important role in carbohydrate metabolism. Low serum and intracellular magnesium levels are associated with insulin resistance, impaired glucose tolerance, and decreased insulin secretion.[12,13]

Magnesium deficiency is significantly more common in patients with T2DM than in the general population, and it is associated with significant morbidity. In particular, low levels of magnesium are associated with diabetic retinopathy and poor glucose control.[14] In fact, some research suggests that supplementation with magnesium, along with other minerals and with vitamins and minerals, can improve glomerular function in patients with T2DM.[15]

Furthermore, several clinical studies indicate a direct relationship between higher magnesium blood levels and improved metabolic control. Among the studies that support these findings are The Women's Health Study, the Health Professionals Follow-up Study and the Nurse's Health Study.[16,17] Many physicians recommend that diabetic patients take at least 400 mg of magnesium daily. When taken as recommended, side effects are rare. The most common side effect is loose stools. If this occurs, the dosage should be reduced.

Omega-3 fatty acids

In the general population, the benefits of fish oil have been well established and can be particularly helpful for patients with diabetes. Omega-3 fatty acids, like those found in anchovies, sardines and salmon, can improve a multitude of parameters in patients with diabetes.

The main effect of omega-3 fatty acids is their ability to lower triglycerides by 20% to 50%.[18] In addition, omega-3 fatty acids have been shown to protect against cardiovascular events. One possible mechanism is the plaque-stabilizing effect that omega-3 fatty acids appear to have on atherosclerotic lesions.

Omega-3 fatty acids have also been linked to reductions in inflammatory cytokines,[19] as well as enhancements in arterial compliance.[20]

Although omega-3 fatty acids do not seem to significantly affect glucose control, there is some evidence that omega-3 fatty acids facilitate the action of insulin. In fact, patients with insulin resistance have a much higher proportion of saturated fatty acids and a lower proportion of polyunsaturated fatty acids in their cell membranes compared with healthy control subjects.

If a patient is taking anticoagulants, coagulation profiles need to be

monitored during supplementation with omega-3-fatty acids. A good starting dosage is 3 g daily with a proper mix of DHA and EPA.[21]

Alpha lipoic acid

Alpha lipoic acid (ALA) is one of the most well-researched nutrients in the treatment of patients with diabetes. ALA has been used as a treatment in Europe for decades. It is a potent fat- and water soluble antioxidant that is synthesized in the body. It is also commonly found in organ meats, brewer's yeast, spinach, broccoli and potatoes. It may help maintain an optimal antioxidant balance within cells by reducing other antioxidants like vitamin C, vitamin E, glutathione and coenzyme CoQ10.[22]

A meta-analysis of four randomized double-blind placebo-controlled trials—-ALADIN I and III, SYDNEY, and the fourth unpublished trial NATHAN II—found a continuous daily improvement in symptoms of peripheral neuropathy such as pain, numbness and tingling.

Several smaller studies confirm the benefit of ALA for patients with diabetic peripheral neuropathy as well. An oral daily dose of 600 mg ALA for three months resulted in reversing symptomatic neuropathy to asymptomatic neuropathy.[23]

When prescribing ALA, patients should be aware that in theory, ALA could have an effect on medications that are metabolized in the liver. Also, it may potentiate hypoglycemia, so insulin and oral hypoglycemic medications may need to be adjusted.

Vitamin C

Vitamin C, ascorbic acid, is a known water-soluble antioxidant. Patients with diabetes excrete excessive amounts of vitamin C through urine. Low levels of vitamin C may make these patients more susceptible to wound infection, delayed healing, endothelial dysfunction and tenosynovial disease.[24]

While many experts believe that correcting subnormal vitamin C levels is beneficial, more data are needed to support this hypothesis. Some promising data were obtained by a group of researchers that found a significant dose-dependent decrease in finger-stick blood sugar, triglycerides, low-density lipoprotein, HbA1c, and serum insulin in the group supplemented with vitamin C.[25]

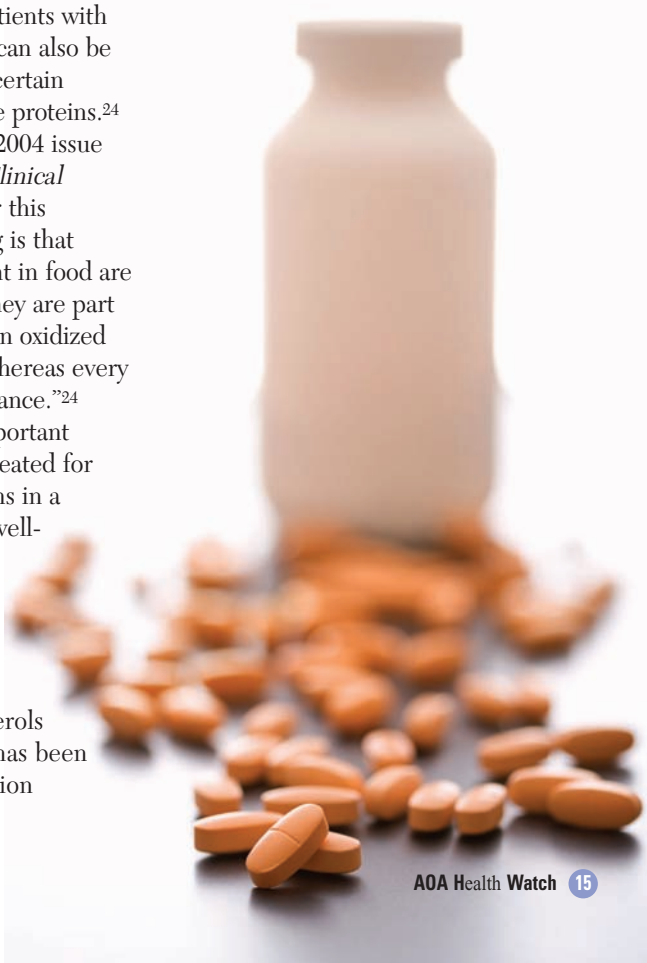
In addition, research has shown that vitamin C supplementation reduces oxidative stress, leading to improved endothelial dysfunction in patients with T2DM. However, vitamin C can also be a pro-oxidant *in vitro* under certain circumstances and can glycate proteins.[24] According to the November 2004 issue of the *American Journal of Clinical Nutrition*, the explanation for this seemingly paradoxical finding is that "antioxidants naturally present in food are balanced biochemically, ie, they are part of a mixture of redox agents in oxidized form and in reduced form, whereas every supplement pill lacks this balance."[24] Therefore, it is extremely important for patients, who are being treated for diabetes, to take their vitamins in a combination formula that is well-balanced, thus providing the antioxidant protection these supplements afford.

Vitamin E:

Vitamin E, or mixed-tocopherols (not d1-alpha-tocopherols), has been shown to prohibit the induction of protein kinase C, which in vascular tissue, is responsible for basement membrane turnover, cellular proliferation and endothelial cell permeability. In the diabetic state, hyperglycemia has been linked to macrovascular and microvascular complications. Vitamin E may prevent or at least delay many of the vascular complications associated with T2DM.[26]

However, there is conflicting evidence regarding the effects of vitamin E. While lower dosages have been shown to improve lipoprotein peroxidizability in humans,[27] some studies have shown that higher dosages seem to have a pro-oxidant effect, similar to that of vitamin C.[28] However, other studies report that this problem with high dosages is not true.[29]

Taking 400 IU daily of vitamin E in the form of natural mixed tocopherols is the recommended way for supplementing with vitamin E. Again, like vitamin C, vitamin E was never meant to be taken in isolation. Patients need to take a variety of



vitamins and minerals to maintain optimal health.

It is unknown whether vitamin E has an additive effect on medications like aspirin.[30] Providers should, therefore, look at coagulation profiles and keep medication interactions in mind when initiating a vitamin E regimen.

Biotin

Biotin is a water-soluble B vitamin that is an essential cofactor in gluconeogenesis, fatty acid synthesis and amino acid catabolism. Humans cannot synthesize biotin, but it can be derived from dietary sources such as peanuts, cooked eggs, soy protein and salmon.

It is thought that biotin stimulates glucose-induced insulin secretion in pancreatic beta cells and accelerates glycolysis in the liver and pancreas, thereby improving abnormal glucose metabolism.[31] Biotin also enhances muscle insulin sensitivity by increasing guanylate cyclase activity.[32] Studies have shown that oral supplementation with 3 mg of biotin three times daily for one month lowered fasting glucose levels by 45% in patients with T2DM for whom sulfonylureas are no longer effective.[33,34]

Some preliminary evidence exists that biotin in high dosages may alleviate diabetic peripheral neuropathy. Within eight weeks of treatment, a marked improvement in paresthesias and muscle cramps occurred, along with a disappearance of restless legs syndrome.[35] In addition, dosages of 10 mg daily have been used successfully to treat peripheral neuropathy.

No biotin toxicity has been reported in individuals supplemented with as much as 200 mg orally or 20 mg intravenously per day.[36]

Ginseng

Because American ginseng is hypothesized to affect carbohydrate metabolism, clinicians have used it in the management of patients with diabetes.

Research suggests that American ginseng attenuates postprandial glycemia, and when taken 40 minutes prior to a meal, significantly lowers blood glucose levels.[37]

Despite ginseng's ability to promote glucose homeostasis, both experimentally and clinically, the mechanism by which this occurs is not completely understood. Some research suggests that American ginseng extracts increase insulin positive cells as well as prevent IL-1beta induced apoptosis in beta cell culture.[38]

Cellular adenosine triphosphate, also known as ATP, levels are closely linked to insulin production and mitochondrial function. American ginseng seems to have the ability to modulate mitochondrial functions and exert an anti-hyperglycemic effect.[38]

The results of several additional studies support the overall *in vivo* antihyperglycemic activity of ginseng in improving the management of patients with T2DM.[37]

The recommended daily ginseng dosage is 1 g to 3 g of the crude root or 200 mg to 600 mg of standardized extract.[39]

Final note

Diabetes can be a devastating disease if patients and physicians do not do all that they can to modify the disease process.

If patients are diligent, they can control their diabetes with diet and exercise alone. Patients must take the lead in preventing the deterioration that can occur if metabolic control is not maintained. With the support of their physicians, patients must fundamentally change their diets, exercise regularly and improve cellular function through supplementation. HW

References

1. Egede L, MD, MS; Ye X, MD, MS; Zheng D, MB, PhD; Silverstein M, MD. The prevalence and pattern of complementary and alternative medicine use in individuals with diabetes. *Diabetes Care.* 2002;25:324-329.
2. Pizzorno J, ND. When patients go alternative. WebMD, LLC, 2007.
3. Mang B, Wolters M, Schmitt B, et al. Effects of cinnamon extract on plasma glucose, HbA1c, and serum lipids in diabetes mellitus type 2. *Eur J Clin Investig.* 2006;36:340-344.
4. Khan A, Safdar M, Ali Khan MM, et al. Cinnamon improves glucose and lipids of people with type 2 diabetes. *Diabetes Care.* 2003;26(12):3215-3218.
5. Ziegenfuss T, Hofheins J, Mendel R, et al. Effects of water-soluble cinnamon extract on body composition and features of the metabolic syndrome in prediabetic men and women. *J Inter Society of Sports Nutrition.* 2006. 3(2); 45-53.
6. Baker WL, Gutierrez-Williams G, White CM, Kluger J, Coleman CI. Effects of cinnamon on glucose control and lipid parameters. *Diabetes Care.* Jan 2008;31(1)41-43.
7. Martin J, Wang Z, Zhang X, Wachtel D, Volaufova J, Matthews D, Cefalu W. Chromium picolinate supplementation attenuates body weight gain and increases insulin sensitivity in subjects with type 2 diabetes. *Diabetes Care.* 2006; 29(8)1826-1832.

8. Anderson RA, Cheng N, Bryden NA, Polansky MM, Chi J, Feng J. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes.* 1997;46:1786-1791.
9. Kleefstra N, Houweling S, Bakker S, Verhoeven S, Gans R, Jong B, et al. Chromium treatment has no effect in patients with poorly controlled, insulin-treated type 2 diabetes in an obese Western population. *Diabetes Care.* 2006;29(3)521-524.
10. Wang ZQ, Qin J, Matin J, Zhang XH, Sereda O, Anderson RA, et al. Phenotype of subjects with type 2 diabetes mellitus may determine clinical response to chromium supplementation. *Metabolism.* 2007;56(12)1652-1655.
11. Cerulli J, Grabe DW, Gauthier I, Malone M, McGoldrick MD. Chromium picolinate toxicity. *The Annals of Pharmacotherapy.* 1998;32(4)428-431.
12. Huerta M, Roemmich J, Kington M, Bovbjerg V, Weltman A, Holmes V, et al. Magnesium deficiency is associated with insulin resistance in obese children. Diabetes Care. 2005;28:1175-1181.
13. Kobrin SM, Goldfarb S. Magnesium deficiency. *Semin Nephrol* 1990; 10:525-35.
14. McNair P, Christiansen C, Madsbad S, et al. Hypomagnesemia, a risk factor in diabetic retinopathy. *Diabetes.* 1978;27:1075-1077.
15. Farvid M, Jalali M, Siassi F, Hosseini M. Comparison of effects of vitamins and/or mineral supplementation on glomerular and tubular dysfunction in type 2 diabetes. *Diabetes Care.* 2005;28:2458-2464.
16. Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects. *Diabetes Care.* 2003;26:1147-52.
17. Guerrero-Romero F, Tamez-Perez HE, Gonzalez-Gonzalez G, Salinas-Martinez AM, Montes-Villarreal J, Trevino-Ortiz JH, et al. Oral magnesium improves insulin sensitivity in non-diabetic subjects with insulin resistance. *Diabetes Metabolism.* 2004;30:253-258.
18. Caterina R, Madona R, Bertolotto A, Schmidt E. N-3 fatty acids in the treatment of diabetic patients. *Diabetes Care.* 2007;30:1012-1026.
19. Meydani S, Endres S, Woods M, Goldin B, Soo C, Morrill-Labrode A, et al. Oral N-3 fatty acid supplementation suppresses cytokine production and lymphocyte proliferation: comparison between young and older women. *Journal of Nutrition.* 1991;121(4):547-555.
20. Mori T, Watts G, Burke V, Hilme E, Puddey I, Beilin L. Differential effects of eicosapentaenoic acid and docosahexaenoic acid on vascular reactivity of the forearm microcirculation in hyperlipidemic, overweight men. *Circulation.* 2000;102:1264.
21. Vessby B, Tengblad S, Lithell H. Insulin sensitivity is related to the fatty acid composition of serum lipids and skeletal muscle phospholipids in 70-year-old men. *Diabetologia.* 1994;37:1044-1050.
22. Hart J, Kracoff G, Ottariono S, Ullmann-Weil M. www.umm.edu. University of Maryland Medical Center Accessed July 19, 2008.
23. Head, K. Peripheral neuropathy: pathogenic mechanisms and alternative therapies. *Alternative Medicine Review.* 2006;11(4).
24. Lee DH, et al. Does supplemental vitamin C increase cardiovascular disease risk in women with diabetes. *American Journal of Clinical Nutrition.* Nov 2004;80(5):1194-2000.
25. Afkhami-Ardekani M, Shojaoddiny-Ardekani A. Effect of vitamin C on blood glucose, serum lipids and serum insulin in type 2 diabetes patients. *Indian J Med Res.* Nov 2007;126(5):471-4.
26. Ruhe RC, McDonald RB. Use of antioxidant nutrients in the prevention and treatment of type 2 diabetes. *Journal of the American College of Nutrition.* 2001;20(5):363S-369S.
27. Engelen W, Keenoy BM, Vertommen J, De Leeuw I. Effects of long-term supplementation with moderate pharmacologic doses of vitamin E are saturable and reversible in patients with type 1 diabetes. *Am J Clin Nutr.* Nov 2000;72(5):1142-9.
28. Winterbone MS, Sampson MJ, Saha S, Hughes JC, Hughes DA. Pro-oxidant effect of alpha-tocopherol in patients with type 2 diabetes after an oral glucose tolerance test—a randomised controlled trial. *Cardiovasc Diabetol.* Feb 22,2007;6:8.
29. Devaraj S, Tang R, Adams-Huet B, Harris A, Seenivasan T, de Lemos JA, et al. Effect of high-dose alpha-tocopherol supplementation on biomarkers of oxidative stress and inflammation and carotid atherosclerosis in patients with coronary artery disease. *Am J Clin Nutr.* Nov 2007;86(5):1392-1398.
30. Chertow B. Advances in diabetes for the millennium: vitamins and antioxidant stress in diabetes and its complications. *MedGenMed.* Nov 2004;6(3 suppl):4.
31. Furukawa Y. Enhancement of glucose-induced insulin secretion and modification of glucose metabolism by biotin. *Nippon Rinsho.* 1999;57:2261-2269.
32. McCarty MF. cGMP may have trophic effects on beta cell function comparable to those of cAMP, implying a role for high-dose biotin in prevention/treatment of diabetes. *Med Hypotheses.* 2006;66:323-328.
33. Maebashi M, Makino Y, Furukawa Y, et al. Therapeutic evaluation of the effect of biotin on hyperglycemia in patients with non-insulin dependent diabetes mellitus. *J Clin Biochem Nutr.* 1993;14:211-218.
34. Coggeshall JC, Heggers JP, Robson MC, Baker H. Biotin status and plasma glucose in diabetics. *Ann NY Acad Sci.* 1985;447:389-392.
35. Koutsikos D, Agroyannis B, Tzanatos-Exarchou H. Biotin for diabetic peripheral neuropathy. *Biomed Pharmacother.* 1990;44:511-514.
36. Mock DM. Biotin. In: *Present Knowledge in Nutrition,* 7th ed. Washington, DC: ILSI Press; 1996:220-235.
37. Attele AS, Zhou YP, Xie JT, Wu JA, Zhang L, Dey L, et al. Antidiabetic effects of panax ginseng berry extract and the identification of effective component. *Diabetes* 2002;51:1851-1858.
38. Zeqi Lou J, Luo L. American ginseng stimulates insulin production and prevents apoptosis through regulation of uncoupling protein-2 in cultures beta cells. *Evidence-based Complementary and Alternative Medicine.* 2006;3(3):365-372.
39. Dey L, Attele AS, Yuan CS. Alternative therapies for type 2 diabetes. *Alternative Medicine Review.* 2002;7(1):45-58.

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