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File: ■ Turmeric (*Curcuma longa*)
■ Curcumin
■ Type 2 Diabetes

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RE: Curcuminoid Extract Lowered the Risk for Type 2 Diabetes Mellitus Development in Prediabetic Subjects

Chuengsamarn S, Rattanamongkolgul S, Luechapudiporn R, Phisalaphong C, Jirawatnotai S. Curcumin extract for prevention of type 2 diabetes. *Diabetes Care*. July 6, 2012;[epub ahead of print]. doi: 10.2337/dc12-0116.

More than 300 million people worldwide have type 2 diabetes mellitus (T2DM), and its prevalence continues to increase. Persons with prediabetes (having blood glucose levels higher than normal but not high enough to be diagnosed as diabetes) can often prevent the development of the disease by making lifestyle changes, but those changes are often challenging. Effective therapeutic agents, with relatively low cost and low toxicity, are needed to control the progression of the disease. Curcumin, the principal curcuminoid in turmeric (*Curcuma longa*), has been shown to possess anti-inflammatory and antidiabetic properties. These authors conducted a randomized, double-blind, placebo-controlled trial to determine the effectiveness of a curcuminoid extract in preventing the development of T2DM.

The 12-month trial was conducted at the HRH Princess Maha Chakri Sirindhorn Medical Center of Srinakharinwirot University in Nakornnayok, Thailand. Eligible subjects were instructed to follow the same protocols for diet and exercise for 3 months after enrollment while awaiting randomization. Standard lifestyle recommendations were provided, and all subjects were counseled one-on-one on the importance of a healthy lifestyle.

Persons aged 35 years and older with prediabetes, as defined by the American Diabetes Association (ADA) guidelines, were included. Eligible subjects had at least 1 of these 3 criteria: fasting plasma glucose (FPG) between 100 mg/dL and 124 mg/dL; an oral glucose tolerance test (OGTT) at 2 hours post-glucose load between 140 mg/dL and 199 mg/dL; and a glycated hemoglobin (Hb_{A1c}) range from 5.7% to 6.4%.

The 237 subjects (with 3 dropouts after randomization) were randomly assigned to either the curcumin-treated group (n=118) or the placebo-treated group (n=116). Baseline characteristics were similar between the 2 groups.

All subjects were instructed to take 3 capsules twice daily for 9 months. The curcuminoid extract was prepared by extracting dried, powdered turmeric with ethanol and removing the oleoresin. Each curcumin capsule contained 250 mg curcuminoids (curcumin, demethoxycurcumin, and bisdemethoxycurcumin in a peak ratio of 1:≤0.6:≤0.4, respectively). Compliance rates were determined by the number of capsules the subjects returned at their follow-up visits at 3, 6, and 9 months.

The primary outcome was the number of subjects in the 2 groups diagnosed with T2DM according to ADA guidelines. Secondary outcomes were changes in β-cell functions (homeostasis model assessment [HOMA]-β, C-peptide, and proinsulin/insulin ratio); insulin resistance (IR) by HOMA-IR; obesity; abdominal obesity; and anti-inflammatory cytokine (adiponectin). β-cells store and release insulin, which controls the level of glucose in the blood.

The authors report that at all visits (months 3, 6, and 9), the diabetes-related blood chemistries (FPG, OGTT at 2 h, and Hb_{A1c}) used to measure the progression of the disease were all significantly lower in the curcumin-treated group compared with the placebo-treated group ($P<0.01$). For example, at month 9, FPG in the curcumin-treated group was 86.47 mg/dL (range=73-122 mg/dL) compared with 108.21 mg/dL (range=80-138 mg/dL) in the placebo-treated group. Mean baseline FPG values were 103.65 mg/dL in the curcumin-treated group and 103.24 mg/dL in the placebo-treated group.

In their assessments of β-cell function, the authors discovered that HOMA-β in the curcumin-treated group was increasingly elevated at all follow-up visits and became statistically significant at month 9 ($P<0.01$). C-peptide levels were significantly lower in the curcumin-treated group compared with the placebo-treated group at 9 months ($P<0.05$). The proinsulin/insulin ratio showed a nonsignificant, lower trend in the curcumin-treated group.

The mean levels of HOMA-IR were lower in the curcumin-treated group than in the placebo-treated group at all visits. The differences were significant at months 6 ($P<0.05$) and 9 ($P<0.001$). Adiponectin levels, unchanged in the placebo-treated group, gradually increased at months 3 and 6 in the curcumin-treated group and became significantly different than the placebo-treated group at month 9 ($P<0.05$).

None of the subjects in either group showed any change in kidney or liver functions. A few subjects in the curcumin-treated group reported minor adverse side effects such as itching, constipation, or vertigo.

The authors report that none of the subjects in the curcumin-treated group developed T2DM in regard to the primary outcome; however, the following numbers of subjects in the placebo-treated group developed T2DM: 11 (9.5%) at month 6; 18 (15.5%) at month 9; and 19 (16.4%) at month 12.

The authors note that the conversion rate of the placebo group was significantly higher than that published in a "well-known" American study.[1] They reasoned that the ethnicity of the subjects in their study may account for the high conversion rate. They compared their results with those of a diabetes study of a large Thai cohort[2] that identified a set of strong risk factors that accelerate the development of T2DM among the Thai population: old age, high body mass index, high waist circumference, hypertension, and a family

history of diabetes. They found that the same factors influenced their study and that their reported rate of development of T2DM was within the estimation of the earlier study.[2] "Therefore, we believe that the high conversion rates found in the present study are a common characteristic of Thai prediabetes," they write.

These authors report that the ethanol-extracted curcuminoids used in this study substantially and significantly prevented T2DM development in subjects with prediabetes. They also found that the curcuminoid extract improved β-cell functions.

"Because of its benefits and safety, we propose that curcumin extract may be used for an intervention therapy for the prediabetes population," they write.

—Shari Henson

References

[1]Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393-403.

[2]Aekplakorn W, Bunnag P, Woodward M, et al. A risk score for predicting incident diabetes in the Thai population. *Diabetes Care*. 2006;29(8):1872-1877.