

Marijuana Use May Protect Against Diabetes

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FROM THE ANNUAL MEETING OF THE AMERICAN PUBLIC HEALTH ASSOCIATION

DENVER – Marijuana use may be associated with a markedly decreased risk of diabetes.

A provocative new analysis of data from the Third National Health and Nutrition Examination Survey (NHANES III) indicates marijuana users had 66%

lower odds of having diabetes after adjustment for numerous potential confounding factors, Dr. Magda Shaheen reported at the meeting.

This robust observed benefit has a biologically plausible mechanism, she noted.

In addition to defects in pancreatic beta-cell function and insulin sensitivity, the pathogenesis of diabetes is thought to involve systemic inflammation. Marijuana contains bioactive cannabinoids that

have been shown to have an anti-inflammatory effect. This was borne out in the NHANES III analysis, where the prevalence of an elevated C-reactive protein level in excess of 0.5 mg/dL was significantly higher in nonusers of marijuana, at 18.9%, than in past users, with a 13% prevalence of elevated CRP, current light users (16%), or current heavy users of the illicit drug (9%), according to Dr. Shaheen of Charles R. Drew University of Medi-

cine and Science, Los Angeles.

The study population consisted of 10,896 NHANES III participants aged 20-59 years; they constituted a statistically representative sample of the broader U.S. civilian population in 1988-1994, when the survey was conducted.

The majority of subjects – 55% – reported never having used marijuana. Another 37% were past users, meaning they hadn't used marijuana during the previous month. The 6% of subjects who reported currently using the drug 1-4 days per month were categorized as current light users, while 3.3% of subjects were current heavier users.

Postmarketing Experience—The following adverse reactions have been identified during postapproval use of FORTEO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- **Osteosarcoma:** Cases of bone tumor and osteosarcoma have been reported rarely in the postmarketing period. The causality to FORTEO use is unclear. Long term osteosarcoma surveillance studies are ongoing.
- **Hypercalcemia:** Hypercalcemia greater than 13.0 mg/dL has been reported with FORTEO use.

Adverse events reported since market introduction that were temporally (but not necessarily causally) related to FORTEO therapy include the following:

- **Allergic Reactions:** Anaphylactic reactions, drug hypersensitivity, angioedema, urticaria;
- **Investigations:** Hyperuricemia;
- **Respiratory System:** Acute dyspnea, chest pain;
- **Musculoskeletal:** Muscle spasms of the leg or back;
- **Other:** Injection site reactions including injection site pain, swelling and bruising; oro-facial edema.

USE IN SPECIFIC POPULATIONS: Pregnancy Category C—There are no adequate and well-controlled studies of FORTEO in pregnant women. In animal studies, teriparatide increased skeletal deviations and variations in mouse offspring at doses more than 60 times the equivalent human dose and produced mild growth retardation and reduced motor activity in rat offspring at doses more than 120 times the equivalent human dose. FORTEO should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In animal studies, pregnant mice received teriparatide during organogenesis at subcutaneous doses 8 to 267 times the human dose. At doses \geq 60 times the human dose, the fetuses showed an increased incidence of skeletal deviations or variations (interrupted rib, extra vertebra or rib). When pregnant rats received subcutaneous teriparatide during organogenesis at doses 16 to 540 times the human dose, the fetuses showed no abnormal findings.

In a perinatal/postnatal study, pregnant rats received subcutaneous teriparatide from organogenesis through lactation. Mild growth retardation in female offspring at doses \geq 120 times the human dose (based on surface area, mcg/m²). Mild growth retardation in male offspring and reduced motor activity in both male and female offspring occurred at maternal doses 540 times the human dose. There were no developmental or reproductive effects in mice or rats at doses 8 or 16 times the human dose, respectively.

Exposure multiples were normalized based on body surface area (mcg/m²). Actual animal doses: mice (30 to 1000 mcg/kg/day); rats (30 to 1000 mcg/kg/day).

Nursing Mothers—It is not known whether teriparatide is excreted in human milk. Because of the potential for tumorigenicity shown for teriparatide in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use—The safety and efficacy of FORTEO have not been established in any pediatric population. FORTEO should not be prescribed in patients at an increased baseline risk of osteosarcoma which include pediatric and young adult patients with open epiphyses. Therefore, FORTEO is not indicated for use in pediatric or young adult patients with open epiphyses.

Geriatric Use—Of the patients receiving FORTEO in the osteoporosis trial of 1637 postmenopausal women, 75% were 65 years of age and over and 23% were 75 years of age and over. Of the patients receiving FORTEO in the osteoporosis trial of 437 men, 39% were 65 years of age and over and 13% were 75 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Hepatic Impairment—No studies have been performed in patients with hepatic impairment.

Renal Impairment—In 5 patients with severe renal impairment (CrCl \leq 30 mL/min), the AUC and T_{1/2} of teriparatide were increased by 73% and 77%, respectively. Maximum serum concentration of teriparatide was not increased.

OVERDOSAGE: Incidents of overdose in humans have not been reported in clinical trials. Teriparatide has been administered in single doses of up to 100 mcg and in repeated doses of up to 60 mcg/day for 6 weeks. The effects of overdose that might be expected include a delayed hypercalcemic effect and risk of orthostatic hypotension. Nausea, vomiting, dizziness, and headache might also occur.

FORTEO® (teriparatide [rDNA origin] injection)

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In postmarketing spontaneous reports, there have been cases of medication errors in which the entire contents (up to 800 mcg) of the FORTEO delivery device (pen) have been administered as a single dose. Transient events reported have included nausea, weakness/lethargy and hypotension. In some cases, no adverse events occurred as a result of the overdose. No fatalities associated with overdose have been reported.

Overdose Management—There is no specific antidote for teriparatide. Treatment of suspected overdose should include discontinuation of FORTEO, monitoring of serum calcium and phosphorus, and implementation of appropriate supportive measures, such as hydration.

DOSAGE FORMS AND STRENGTHS: Multi-dose prefilled delivery device (pen) for subcutaneous injection containing 28 daily doses of 20 mcg.

PATIENT COUNSELING INFORMATION: Patients should read the FDA-approved *Medication Guide* and delivery device (pen) *User Manual* before starting therapy with FORTEO and re-read them each time the prescription is renewed. Patients need to understand and follow the instructions in the FORTEO delivery device *User Manual*. Failure to do so may result in inaccurate dosing.

PLEASE SEE FULL PRESCRIBING INFORMATION FOR ADDITIONAL INFORMATION.

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VITALS Major Finding: The age-adjusted prevalence of diabetes was 4% in nonusers and significantly lower at 3% in marijuana users. In a multiple logistic regression analysis adjusted for sociodemographic factors, comorbid conditions, laboratory values, and inflammatory markers, marijuana users had a 66% lower likelihood of having diabetes.

Data Source: A cross-sectional study involving 10,896 NHANES III participants aged 20-59 years.

Disclosures: The study was funded by Omics Biotechnology, which is pursuing potential medical applications for nonpsychotropic cannabinoid receptor agonists. Dr. Shaheen declared she has no relevant financial relationships.

The age-adjusted prevalence of diabetes in this cross-sectional study was 4% in nonusers and significantly lower at 3% in marijuana users.

Current and past users of marijuana were significantly younger, had a lower body mass index, and were more physically active than were nonusers. They were also more likely to smoke cigarettes, drink alcohol, and use cocaine. In addition, they were more likely to have an HDL level greater than 40 mg/dL and had lower mean total cholesterol, LDL, and triglyceride levels.

In a multiple logistic regression analysis adjusted for sociodemographic factors, comorbid conditions, laboratory values, and inflammatory markers, marijuana users had a 66% lower likelihood of having diabetes. This benefit was confined to the 41- to 59-year-old age group, where the reduction in diabetes risk associated with marijuana use was 67%. In contrast, the 7% reduction in risk among 20- to 40-year-olds was not statistically significant. These findings could be the result of the markedly higher occurrence of diabetes in middle age.

Unlike in diabetes, marijuana use was not associated with a lower prevalence of the other chronic diseases that Dr. Shaheen and coworkers looked at in which systemic inflammation also plays a role: myocardial infarction, heart failure, stroke, and hypertension. "This was probably due to the lower prevalence of these diseases in this age group," she commented. ■