

OA Patients at Substantial Cardiovascular Risk

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ROME – Cardiovascular risk profiles in osteoarthritis patients are, on average, comparable with those in patients with rheumatoid arthritis, according to a Dutch study.

In recent years, much attention has been focused on the elevated risk of car-

diovascular events in patients with rheumatoid arthritis, as a consequence of their increased prevalence of the standard cardiovascular risk factors coupled with a further boost in risk resulting from the chronic systemic inflammatory disease process.

The cardiovascular risk associated with osteoarthritis has received far less attention, Dr. Inger Meek observed.

She determined the cardiovascular risk

profiles of 285 consecutive rheumatoid arthritis patients and 112 consecutive osteoarthritis patients using the SCORE (Systematic Coronary Risk Evaluation) system, which is routinely employed in European clinical practice in lieu of the Framingham risk score.

The two populations were similar in terms of mean age and sex. The mean disease duration of the rheumatoid arthritis patients was 6.8 years.

In all, 18% of the osteoarthritis patients in the study had a greater-than-10% estimated 10-year risk of a fatal cardiovascular event by SCORE, as did 15% of rheumatoid arthritis patients, according to Dr. Meek, who is with the University of Twente in Enschede, the Netherlands.

Hypercholesterolemia was significantly more prevalent in the osteoarthritis patients, by a margin of 45%, compared with 29% for the rheumatoid arthritis patients.

The two groups did not differ significantly in terms of the other elements of SCORE (smoking status, systolic blood pressure, age, and sex).

The SCORE system, developed by the European Society of Cardiology, is based upon 3 million person-years of observation, and doesn't factor in body mass index, Dr. Meek noted.

18% of the osteoarthritis patients in the study had a greater-than-10% estimated 10-year risk of a fatal cardiovascular event, as did 15% of RA patients.

Obesity is a well-established cardiovascular risk factor, and its prevalence is greatly increased in patients with osteoarthritis. Thus, SCORE likely underestimates their true cardiovascular mortality risk.

Recent evidence-based recommendations by the European League Against Rheumatism advise physicians to apply a 1.5 multiplication factor to the conventional cardiovascular mortality risk SCORE in rheumatoid arthritis patients who meet two of three criteria: disease duration greater than 10 years, rheumatoid factor or anti-cyclic citrullinated peptide positivity, or extra-articular disease manifestations (*Ann. Rheum. Dis.* 2010;69:325-31).

This is designed to account for the heightened cardiovascular risk imposed by a high degree of systemic inflammation.

The substantial percentage of osteoarthritis patients in this study who had a greater-than-10% estimated likelihood of cardiovascular death within 10 years is of particular concern, Dr. Meek stressed, because the prevalence of osteoarthritis is expected to mushroom in the near future as a result of the graying of the baby boom generation.

Dr. Johannes W.J. Bijlsma of the University Medical Center Utrecht (the Netherlands) commented that the take-home message of Dr. Meek's study is that physicians need to be aware that it's not only their rheumatoid arthritis patients but also their osteoarthritis patients who are at increased cardiovascular risk.

Dr. Meek declared having no financial conflicts. ■

LANTUS®

(insulin glargine [rDNA origin] injection) solution for subcutaneous injection

The following are examples of drugs that may increase the blood-glucose-lowering effect of insulins including LANTUS and, therefore, increase the susceptibility to hypoglycemia: oral anti-diabetic products, pramlintide, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, propoxyphene, pentoxifylline, salicylates, somatostatin analogs, and sulfonamide antibiotics.

The following are examples of drugs that may reduce the blood-glucose-lowering effect of insulins including LANTUS: corticosteroids, niacin, danazol, diuretics, sympathomimetic agents (e.g., epinephrine, albuterol, terbutaline), glucagon, isoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), protease inhibitors and atypical antipsychotic medications (e.g. olanzapine and clozapine).

Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

The signs of hypoglycemia may be reduced or absent in patients taking sympatholytic drugs such as beta-blockers, clonidine, guanethidine, and reserpine.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rats and Himalayan rabbits. Insulin glargine was given to female rats before mating, during mating, and throughout pregnancy at doses up to 0.36 mg/kg/day, which is approximately 7 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 mg/kg/day), based on mg/m². In rabbits, doses of 0.072 mg/kg/day, which is approximately 2 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 mg/kg/day), based on mg/m², were administered during organogenesis. The effects of insulin glargine did not generally differ from those observed with regular human insulin in rats or rabbits. However, in rabbits, five fetuses from two litters of the high-dose group exhibited dilation of the cerebral ventricles. Fertility and early embryonic development appeared normal.

There are no well-controlled clinical studies of the use of LANTUS in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is essential for patients with diabetes or a history of gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. Insulin requirements may decrease during the first trimester, generally increase during the second and third trimesters, and rapidly decline after delivery. Careful monitoring of glucose control is essential in these patients.

8.3 Nursing Mothers

It is unknown whether insulin glargine is excreted in human milk. Because many drugs, including human insulin, are excreted in human milk, caution should be exercised when LANTUS is administered to a nursing woman. Use of LANTUS is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their insulin doses.

8.4 Pediatric Use

The safety and effectiveness of subcutaneous injections of LANTUS have been established in pediatric patients (age 6 to 15 years) with type 1 diabetes [see *Clinical Studies (14) in the full prescribing information*]. LANTUS has not been studied in pediatric patients younger than 6 years of age with type 1 diabetes. LANTUS has not been studied in pediatric patients with type 2 diabetes.

Based on the results of a study in pediatric patients, the dose recommendation when switching to LANTUS is the same as that described for adults [see *Dosage and Administration (2.3) and Clinical Studies (14) in the full prescribing information*]. As in adults, the dosage of LANTUS must be individualized in pediatric patients based on metabolic needs and frequent monitoring of blood glucose.

8.5 Geriatric Use

In controlled clinical studies comparing LANTUS to NPH insulin, 593 of 3890 patients (15%) with type 1 and type 2 diabetes were ≥65 years of age and 80 (2%) patients were ≥75 years of age. The only difference in safety or effectiveness in the subpopulation of patients ≥65 years of age compared to the entire study population was a higher incidence of cardiovascular events typically seen in an older population in both LANTUS and NPH insulin-treated patients.

Nevertheless, caution should be exercised when LANTUS is administered to geriatric patients. In elderly patients with diabetes, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in the elderly [See *Warnings and Precautions (5.3)*].

10. OVERDOSAGE

An excess of insulin relative to food intake, energy expenditure, or both may lead to severe and sometimes prolonged and life-threatening hypoglycemia. Mild episodes of hypoglycemia can usually be treated with oral carbohydrates. Adjustments in drug dosage, meal patterns, or exercise may be needed.

More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. After apparent clinical recovery from hypoglycemia, continued observation and additional carbohydrate intake may be necessary to avoid recurrence of hypoglycemia.

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