Health and Drug Alerts

Rosiglitazone (Avandia) and macular edema

Reason for posting: Thiazolidinediones such as rosiglitazone are insulin sensitizers used in the treatment of type 2 diabetes and polycystic ovarian disease. Some patients taking these drugs experience peripheral edema. Recent advisories have noted that patients may also experience visual disturbances related to macular edema.

The condition: Macular edema occurs when the blood vessels leak plasma into the surrounding retina. Among people with type 2 diabetes, it can be found in 15% of those who use insulin and 4% of those who do not. Risk factors for macular edema and its symptoms are listed in Box 1.

Cases of rosiglitazone-related macular edema were first described in September 2005. The manufacturer of the drug, GlaxoSmithKline, announced subsequently that the effect had been reported in an undisclosed number of postmarketing cases worldwide. Although limited clinical data on affected patients are available from GlaxoSmithKline or Health Canada, most of the patients affected were reported also to have fluid retention, peripheral edema or weight gain. Key unreported case details included the patients' ages, duration of diabetes, doses and duration of rosiglitazone use, concomitant medication use and occurrence, if any, of pre-existing diabetic retinopathy. Some patients improved after rosiglitazone use was discontinued.

Health Canada has received 9 reports of visual impairment in patients taking rosiglitazone. Of these, only one was clearly associated with macular edema: a 65-year-old woman who had taken an unspecified dosage for more than a year. Her symptoms, which also included hypertension and peripheral edema (but no retinopathy), resolved upon discontinuation of the drug (Barbara Raymond, Marketed Pharmaceuticals Division, Health Canada: personal communication, 2006).

The patients who appear to be at greatest risk of peripheral edema, fluid retention and weight gain, congestive heart failure and pulmonary edema related to rosiglitazone are those who use insulin or have New York Heart Association class II, III or IV cardiac status, left-ventricular dysfunction or renal insufficiency. These effects are dose-related. Although the exact cause of macular edema is unknown, thiazolidinediones are hypothesized to cause peripheral edema by affecting renal and intestinal ion transport, increasing plasma volume and sympathetic activation, and causing growth factor–related vascular permeability.

What to do: Although rosiglitazone-related macular edema is rare, patients using the drug should be advised to seek immediate medical attention if they begin to experience visual symptoms (Box 1). Consider discontinuing the medication if macular edema occurs. Asymptomatic macular edema is likely to be noted at a patient's yearly ophthalmologic screening for diabetic retinopathy. Individual patients' risk factors for macular edema, such as poor glycemic control and hypertension, should be optimized according to existing guidelines.

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REFERENCES
1. Wooltorton E. Rosiglitazone (Avandia) and pioglitazone (Actos) and heart failure. CMAJ 2002;166(3):219.

Box 1: Macular edema
Risk factors
• Longstanding diabetes
• Insulin use
• Diabetic retinopathy
• Hypertension
• Poor glycemic control
Symptoms
• Blurred or distorted vision
• Decreased colour sensitivity
• Decreased dark adaptation

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