Glitazones and Heart Failure: Critical Appraisal for the Clinician

To the Editor:

I would like to add my clinical observations to the excellent scientific review of heart failure and “glitazone” drugs by Wang et al.1 Symptomatic peripheral edema is quite common in insulin-treated patients in whom glitazones are added (~15% in the rosiglitazone2 and pioglitazone3 clinical trials) and occasionally profound, even presenting as anasarca.4 When severe, it usually starts within 3 to 4 weeks, often before a significant change in glycemia. The most common echocardiographic finding is diastolic dysfunction, generally with normal systolic performance.

The frequency at which I have encountered problems with edema has been much reduced by developing relatively rigid prescribing habits, which I would like to share.

Always check for edema before prescribing a glitazone. In patients with even trace edema, demonstrate to patients how to check themselves and request their doing so nightly. Suggest that they call or stop the glitazone if edema or dyspnea develops. When prescribing glitazones in patients at higher risk for developing edema (insulin treated or with pre-existing edema, known vascular disease, multiple cardiac risk factors, or a history of heart failure), start with pioglitazone 15 mg or rosiglitazone 2 mg daily and ask the patient to return in 1 month. If the patient does not develop edema or improved glycemia, double the dose of glitazone; if glycemia is improved, wait 2 to 3 months before titrating as necessary. Do not increase the dose to maximum levels in high-risk patients unless there has been virtually no response with respect to fluid status or glycemia at intermediate doses. In patients with risk factors for the development of edema, try to avoid the use of dihydropyridine calcium channel blockers and high-dose or daily nonsteroidal anti-inflammatory drugs.

If the patient develops symptomatic fluid retention, ask about salt content of foods and explore whether substantial lifestyle changes can be made and sustained. If not, initiate therapy with a thiazide diuretic or add a loop diuretic to those already on thiazide for blood pressure control. If the patient has already initiated or increased diuretic therapy, assess intravascular volume by examining orthostatic vital signs as well as serum chemistries before considering further diuresis. If the addition of diuretics does not rapidly improve symptoms, reduce the glitazone dose by 50% by splitting the prescribed tablet in half for 2 to 3 weeks if symptoms are modest, or consider discontinuing therapy.

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