



Rosiglitazone and macular edema

As noted in Box 1 in the article by Claire Kendall and Eric Wooltorton,¹ long-standing diabetes mellitus, poor diabetes control and insulin therapy are by themselves risk factors for macular edema. Furthermore, only 1 of the 9 cases of visual impairment reported in Canada for patients taking rosiglitazone was clearly associated with macular edema, and in that case the problem was resolved by discontinuation. The questions thus arise of whether macular edema (especially if it is asymptomatic) is an absolute contraindication to rosiglitazone therapy and whether every patient with diabetes must be subjected to ophthalmologic evaluation before starting this drug.

Although adverse symptoms may diminish upon discontinuation of rosiglitazone, the potential for loss of glycemic control must also be considered. In such situations, what is the risk-benefit ratio for continuation of rosiglitazone therapy, especially if good glycemic control has been achieved?

Perhaps there is a role for “drug holidays” with rosiglitazone. In this regard, macular edema induced by latanoprost, echthiophate iodide or nicotinic acid is usually reversible upon discontinuation of the drug,² which can be reintroduced later.

Systemic factors that may contribute to the progression of diabetic macular edema are blood glucose control, hy-

pertension, nephropathy and proteinuria. It has been suggested that use of an angiotensin-converting enzyme (ACE) inhibitor be considered for patients with diabetic retinopathy and nephropathy.³ ACE inhibitors are already indicated for microalbuminuria of diabetes, but it is not known whether they would be beneficial in preventing macular edema as well.

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SMART therapy

The Salmeterol Multicenter Asthma Research Trial (SMART)¹ reinforces important lessons regarding the appropriate use of long-acting β -agonists. The trial was stopped early because of increased hazard of asthma, respiratory death or life-threatening events in the salmeterol arm. Eric Wooltorton's Health and Drug Alert² based on data from this study warns physicians of this hazard but fails to put the results in the context of the greater body of research examining the role of long-acting β -agonists in asthma.

Studies examining the use of these drugs in combination with inhaled corticosteroids have consistently demonstrated benefit, with significant reductions in severe asthma exacerbations.³⁻⁶ Furthermore, the SMART trial failed to

show a significant hazard in patients using inhaled corticosteroids at baseline. Despite this, Wooltorton discounts the role of inhaled corticosteroids as a determinant of outcome, stating “Although there is interest in attributing differences in outcomes to differences in baseline rates of inhaled corticosteroid use at enrolment, the trials were not adequately designed to assess this.”

Although this statement is true, the message is not. The Canadian asthma consensus guidelines,⁷ in agreement with recommendations worldwide, emphasize the need for adequate anti-inflammatory therapy before starting add-on treatment, including long-acting β -agonists. This was not the case in the SMART trial.

Administration of long-acting β -agonists in combination with inhaled corticosteroids, preferably in a single inhalation device, remains the most effective strategy for prevention of severe asthma exacerbations in those with persistent disease. If we are to reduce asthma morbidity and mortality, it is critical for this message to be understood by clinicians and not confused by reports of inappropriate use.

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