Review: Rosiglitazone or pioglitazone as add-on therapy is effective for glycemic control in type 2 diabetes

Boucher M, McAuley L, Brown A, Keely E, Skidmore B. **Efficacy of rosiglitazone and pioglitazone compared to other anti-diabetic agents: systematic review and budget impact analysis.** Technology report no. 29. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); Oct 2002. http://www.ccohta.ca.

QUESTION

In patients with type 2 diabetes mellitus, is rosiglitazone or pioglitazone more effective than other antidiabetic agents when used either as monotherapy or add-on therapy?

DATA SOURCES

Studies were identified by searching 7 databases and Web sites of regulatory and health technology–assessment agencies, reviewing bibliographies of selected articles, and contacting manufacturers.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) comparing rosiglitazone or pioglitazone, as monotherapy or as add-on therapy, with other antidiabetic agents in patients > 18 years of age with type 2 diabetes.

DATA EXTRACTION

Data were extracted independently by 2 reviewers on study quality using the Jadad 5-point scale, study length, comparator drug, dosage, and results. The main outcomes were mean differences from baseline to endpoint in glycosylated hemoglobin (HbA_{1c}) and fasting plasma glucose (FPG) levels.

MAIN RESULTS

11 RCTs of rosiglitazone and 8 RCTs of pioglitazone met the selection criteria. 2 RCTs of rosiglitazone monotherapy could be pooled: Rosiglitazone decreased FPG but not HbA_{1c} levels more than glyburide or repaglinide (Table). Pooling among add-on therapy studies showed rosiglitazone decreased HbA_{1c} (8 RCTs) and FPG (7 RCTs) levels more than continuing monotherapy with a nonthiazolidinedione agent (Table). 2 trials of monotherapy with pioglitazone that could be pooled showed less decrease in HbA_{1c} levels with pioglitazone than with glyburide or repaglinide (Table). 1 trial showed a nonsignificantly smaller decrease in FPG level with pioglitazone monotherapy than with repaglinide (Table). Add-on therapy with pioglitazone decreased HbA_{1c} (6 RCTs) and FPG (5 RCTs) levels more than nonthiazolidinedione monotherapy (Table).

CONCLUSIONS

In patients with type 2 diabetes, little evidence exists to support rosiglitazone or pioglitazone being more effective monotherapy than existing antidiabetic agents. When added to a nonthiazolidinedione agent, both drugs reduce glycosylated hemoglobin and fasting plasma glucose levels more than monotherapy with a nonthiazolidinedione agent.

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Rosiglitazone (Ros) or pioglitazone (Pio) vs other antidiabetic drugs for type 2 diabetes mellitus*

Outcomes	Interventions	Number of trials	Study duration (wk)	Weighted mean difference (95% CI)
HbA_{1c} (%)	Ros monotherapy	2	24 to 52	–0.08 (–0.65 to 0.49)†
	Pio monotherapy	2	24 to 26	0.46 (0.03 to 0.90)
	Ros add-on	8	24 to 26	–1.29 (–1.37 to –1.22)
	Pio add-on	6	12 to 24	–1.29 (–1.60 to –0.99)
FPG (mmol/L)	Ros monotherapy	2	24 to 52	–0.62 (–1.07 to –0.17)
	Pio monotherapy	1	24	0.89 (–0.26 to 2.04)†
	Ros add-on	7	24 to 26	–2.82 (–3.15 to –2.48)
	Pio add-on	5	12 to 24	–2.87 (–3.59 to –2.15)

*HbA_{1c} = glycosylated hemoglobin; FPG = fasting plasma glucose. CI defined in Glossary. A random-effects model was used.
†Not significant.

COMMENTARY

Type 2 diabetes is a progressive condition, which demands a stepped therapeutic approach from lifestyle changes alone, to addition of 1 or more oral glucose-lowering drugs, to combination with insulin.

Peroxisome proliferator-activated receptor-γ (PPAR-γ) agonists, such as rosiglitazone and pioglitazone, have the potential to be true antidiabetic (rather than glucose-lowering) drugs. But until longer-term studies are concluded, their potential cannot be fully recognized in clinical practice. These drugs are expensive, and it is clear from the review by Boucher and colleagues (and others before it [1, 2]) that they show no advantage in cost-effectiveness over metformin or sulfonylurea monotherapy.

Clearly, however, this review confirms that PPAR-γ agonists have considerable glucose-lowering efficacy when added to a glucose-lowering drug. Although the data do not show whether this is also true as add-on to any 2-drug combination, there seems little reason for doubt. Use of these drugs, clinically most effective in people with overt metabolic syndrome, may be an alternative to add-on insulin therapy.

Boucher and colleagues showed that the introduction of thiazolidinediones can have an important effect on the budget of publicly funded drug programs in Canada. A full economic analysis to help better understand the true costs of rosiglitazone and pioglitazone is not available.

Putting the review in the context of current clinical need and practice, PPAR-γ agonists could be considered appropriate add-on therapy in patients already taking oral glucose-lowering therapy, or as monotherapy where oral glucose-lowering drugs are not tolerated. The precise role of PPAR-γ agonists in combination with insulin injections has yet to be established.

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References

1. Guidance on Rosiglitazone for Type 2 Diabetes Mellitus. National Institute for Clinical Excellence. www.nice.nhs.uk.
2. Guidance on Pioglitazone for Type 2 Diabetes Mellitus. National Institute for Clinical Excellence. www.nice.org.uk/.