Worldwide experience of metformin as an effective glucose-lowering agent: a meta-analysis
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Authors' objectives
To assess the efficacy of metformin compared to sulphonylurea(s) as a first-line treatment of non-insulin dependent diabetes mellitus, when diet alone has failed to control blood glucose.

Searching
MEDLINE, EMBASE, Pascal and BIOSIS Previews were searched from January 1957 to September 1994 in all languages with the keywords terms: ‘metformin’, ‘sulphonylureas’ and ‘humans’. Major diabetic and endocrinology textbooks and review articles were also studied.

Study selection
Study designs of evaluations included in the review
Published randomised controlled trials (RCTs). Crossover or non-crossover, open or blinded with a minimum duration of treatment of 6 weeks.

Specific interventions included in the review
Metformin and sulphonylurea(s) for the treatment of non-insulin dependent diabetes mellitus.

Participants included in the review
Patients with non-insulin dependent diabetes mellitus, either newly presenting or with long-standing diabetes up to 24 years. Age ranged from 36 to 94 years and the majority of patients were overweight.

Outcomes assessed in the review
Glycaemic control (assessed by fasting plasma glucose, random plasma glucose or glycated haemoglobin) and body weight details. Other outcome measures included C-peptide, plasma insulin, serum triglycerides and total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined by a meta-analysis, with the study means weighted by sample size.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.
Results of the review
Eleven RCTs involving 651 patients were included.

There were 14 and 19% reductions in fasting plasma glucose with metformin and sulphonylurea respectively. There was a similar 44.5% reduction in the post-prandial glucose levels with both groups of drugs. Both the metformin and sulphonylurea treatments resulted in a reduction in glycated haemoglobin of 1.25% (a 12.5% fall). In the 9 studies which reported it, there was no significant change in body weight for any of the studies with sulphonylurea therapy, compared with 7 studies for metformin therapy. Overall there was a 4 kg weight differential in the metformin treated subjects (-1.2 versus +2.8 kg) representing a 5% net difference between agents. Side-effects led to the withdrawal of 3% of patients on metformin due to gastrointestinal symptoms, and less than 1% on sulphonylureas because of symptoms of hypoglycaemia.

Authors' conclusions
Metformin is equally as efficacious as the sulphonylureas, with a resultant 1.2% fall in glycated haemoglobin for both drugs. However, as most type-2 diabetic patients are overweight, the net 5% reduction in weight reduction in favour of metformin may be of benefit in the management of the insulin resistant syndrome associated with non-insulin dependent diabetes mellitus.

CRD commentary
There were several inconsistencies in the published review, for example, the results from figure 2 are inconsistent with the discussion of them in the text. Confidence intervals or results of tests of statistical significance were not reported and clinical significance of the differences found were not discussed. Only 9 of the 11 studies included provided body weight details, although this was one of the inclusion criteria. The exclusion of unpublished studies and abstracts may influence the estimated treatment effect due to publication bias.

One author was affiliated to Lipha Pharmaceuticals Ltd.

Bibliographic details

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract
contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.